ABSTRACTS

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American College of Clinical Pharmacy
2003 Annual Meeting
November 2–5 • 2003
Hyatt Regency Atlanta
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Encore Presentations: Abstracts marked with an "E" are Encore Presentations. Encore Presentations undergo the same peer review process as do Original Presentations, but may have been presented elsewhere or published in abstract form only prior to the 2003 Annual Meeting. For Encore Presentations, the abstract title, authors, and original citation (if provided) are published in *Pharmacotherapy*. The full abstract will be published in the meeting program book.

ORIGINAL RESEARCH

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

Administration

1. Manifesto on pharmaceutical clinical technology: a conceptual-theoretical-empirical system of knowledge for guiding pharmacy practice, education, and research. Ari Heller, M.D. Jacqueline Fawcett, Ph.D., Albert Wertheimer, Ph.D., *David Hawkins, Pharm.D.,* Gary Matzke, Pharm.D., Chris Bradberry, Pharm.D., the PCT Collaborative Study Group; Creighton University, Omaha, NE; Temple University, Philadelphia, PA; University of Massachusetts, Boston, MA; University of Pittsburgh, Pittsburgh, PA.

PURPOSE: The purpose of the manifesto is to provide a medical, scientific, educational, professional, and legal basis for expanding the scope of pharmacy practice by including pharmaceutical clinical technology (PCT). PCT is the rational, effective, safe, and cost efficient use of medical technologies (e.g., devices, instruments, single use items, biotech, and diagnostics) and medications in the prevention, treatment, and diagnosis of human disease.
METHODS: The manifesto on PCT was created using the conceptual-theoretical-empirical systems approach described by Fawcett. This method involves defining those elements of practice that are unique to the discipline, establishing the theoretical basis upon which the discipline is practiced, and describing the empirical tools used in the day-to-day performance of professional activities. This collaborative inquiry process was undertaken by a multidisciplinary team and then subjected to the critical review of over 150 senior experts from the fields of pharmacy, medicine, and biomedical engineering. In addition, the evolving manifesto was subjected to the critical review of more than 10 experts in pharmacy law.
RESULTS: A vigorously revised and highly refined document was generated that provides a clear conceptual-theoretical-empirical system of knowledge for guiding pharmacy practice, research, and education. To date, two schools of pharmacy have adopted the PCT manifesto.
CONCLUSIONS: A manifesto which calls for the implementation of pharmaceutical clinical technology as a means of expanding the scope of pharmacy practice and for establishing a conceptual-theoretical-empirical basis for pharmacy practice, education, and research is gaining wide acceptance among academic and practicing pharmacists world-wide.

Adverse Drug Reactions/Drug Interactions

2E. No influence of alcohol intake on the pharmacokinetics or pharmacodynamics of the oral direct thrombin inhibitor ximelagatran in healthy volunteers. *Kajs-Marie Schutzer, M.D., Ph.D.,* Susanne Johansson, M.Sc., Eva Kessler, M.Sc., Troy C. Sarich, Ph.D., Ulf G. Eriksson Ph.D.; AstraZeneca R&D Molndal, Molndal, Sweden; AstraZeneca LP, Wilmington, DE.

Presented at the XIX Congress of the International Society on Thrombosis and Hemostasis, Birmingham, United Kingdom, July 12-18, 2003.

3E. Influence of Levitra™ (vardenafil) 10 mg and 20 mg on aspirin®-induced prolongation of bleeding time in normal healthy males. *Arthur Mazzu, Ph.D.,* Prabhu Rajagopalan, Ph.D.; Bayer Healthcare, West Haven, CT.

Presented at the Annual Meeting of the Canadian Cardiovascular Congress, October 25-29, 2003, Toronto, ON, Canada.

4E. Pharmacodynamic interactions of vardenafil 20 mg: a selective phosphodiesterase-5 inhibitor, with sublingual nitroglycerin in healthy middle-aged male subjects. *Arthur Mazzu, Ph.D.,* Miguel Zinny, M.D., Andrew Nicholls, M.D., PhD, Pavur Sundaresan, M.D., Ph.D.; Bayer Healthcare, West Haven, CT; ProMedica Clinical Research Center, Inc., Brighton, MA.

Presented at the Annual Meeting of the American Heart Association, Orlando, FL, November 2-5, 2003.

5E. No clinically significant interaction between ximelagatran, an oral direct thrombin inhibitor, and amiodarone. *Renli Teng, Ph.D.,* Troy C. Sarich, Ph.D., Ulf G. Eriksson, Ph.D., Jennifer E. Hamer, M.Sc., Stephen Gillette, Kajs-Marie Schutzer, M.D., Ph.D., Glenn F. Carlson, Jr., M.D., Peter R. Kowey, M.D.; AstraZeneca LP, Wilmington, DE; AstraZeneca R&D Molndal, Molndal, Sweden; Lankenau Hospital, Wynnewood, PA.

Presented at the Annual Meeting of the European Society of Cardiology, Vienna, Austria, August 30-September 3, 2003.

6. Moxifloxacin-induced hepatitis. *Corinne Chahine, B.S., Pharm.D.,* Henry Cohen, M.S., Pharm.D., Rajat Mukherji, M.D., Gerardo Garcia, M.D.; Kingsbrook Jewish Medical Center, Brooklyn, NY.

BACKGROUND: Fluoroquinolones are associated with variable degrees of hepatotoxicity, some of which were fatal as was seen with trovafloxacin. From pre-marketing clinical research with moxifloxacin, approved in December 1999, elevations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) up to 3 times the upper limit of normal, were reported in 7% of moxifloxacin-treated patients (> 4900) with no cases of acute hepatic failure. A MEDLINE search through May 2003, revealed one case of a reversible moxifloxacin-induced acute cholestasis. We report a possible case of moxifloxacin-induced hepatitis.
CASE SUMMARY: An 85-year-old black female was started on parenteral moxifloxacin 400 mg QD for empirical pneumonia therapy. Her past medical history included hypertension, diabetes, chronic heart failure and chronic obstructive pulmonary disease. She was receiving digoxin, furosemide and atorvastatin for years. Upon hospital admission, baseline hepatic profile was normal. On day 5 of moxifloxacin therapy, AST and ALT gradually increased to 1301 and 1430 U/L, respectively. Other liver test abnormalities revealed elevated ammonia (1.99 µg/ml), bilirubin (2.3 md/dL) and international normalized ratio (2.44). All medications were then discontinued. Alcoholic, viral, obstructive or autoimmune mediated hepatitis were ruled out. Abdominal sonogram revealed fatty liver infiltrates. Liver biopsy was not performed. AST and ALT continued increasing through day 9, exceeding 2000 U/L. From days 10 through 14, AST and ALT decreased to 68 and 203 U/L, respectively. The patient expired on day 20 of hospital stay.
CONCLUSIONS: The temporal relationship between moxifloxacin and the onset of hepatitis favors this drug as a culprit.

7. Effect of eplerenone on the pharmacokinetics of an oral contraceptive agent. *Susan E. Reid, M.Ed.,* Dwain S. Tolbert, Ph.D., Scott Krause, B.S.N.; Pfizer Corporation, Skokie, IL; Takeda Pharmaceuticals, Lincolnshire, IL.

PURPOSE: Eplerenone, a selective aldosterone blocker, reduces blood pressure in patients with mild to moderate hypertension. This study evaluated the effect of steady-state eplerenone (100 mg QD for 11 days) on an oral contraceptive, norethindrone/ethinyl estradiol (Ortho-Novum 1/35) in healthy adult females.
METHODS: Single blind, two-period, placebo-controlled, crossover design trial in 24 healthy female subjects. Subjects received one 28-day treatment of oral contraceptive tablets coadministered with placebo tablets QD, and one 11-day treatment of oral contraceptive tablets coadministered with eplerenone 100 mg QD.
RESULTS: Compared to placebo, coadministration of eplerenone (100 mg QD), did not clinically significantly affect the overall plasma exposure (AUC_{0-24}) of ethinyl estradiol (-0.6%) or norethindrone (+16.7%). Eplerenone coadministration did not clinically significantly affect sex hormone binding globulin (SHBG). Coadministration of eplerenone with the oral contraceptive was safe and well tolerated.
CONCLUSIONS: Eplerenone did not induce the metabolism of either the progestational (norethindrone) or the estrogenic (ethinyl estradiol) component of a combination oral contraceptive agent. Coadministration of eplerenone with oral contraceptives therefore does not increase the risk of pregnancy.

8. Pharmacokinetics of eplerenone coadministered with glyburide and its effect on glyburide pharmacodynamics. *Susan E. Reid, M.Ed.,* Dwain S. Tolbert, Ph.D., James Ferry, Ph.D., Scott Krause, B.S.N.; Pfizer Corporation, Skokie, IL; Takeda Pharmaceuticals, Lincolnshire, IL.

PURPOSE: Hypertensive patients often have additional medical conditions such as diabetes that necessitate pharmacologic intervention. This trial evaluated the pharmacokinetics and pharmacodynamics of glyburide coadministered with eplerenone, a selective aldosterone blocker.
METHODS: Single-blind, randomized, two treatment, two period, placebo-controlled, crossover design trial in 16 type 2 diabetic patients given multiple doses of eplerenone (100 mg QD) coadministered with glyburide 5 mg QD (n=8) and 10 mg BID (n=8).
RESULTS: Insulin overall exposure ($AUC_{0\text{-}24}$) and average exposure (C_{ave}) in the 10 mg BID glyburide group increased by approximately 22% and 21%, respectively, whereas for the 5 mg QD group, insulin $AUC_{0\text{-}24}$ and C_{ave} increased 17% and 20%, respectively. Glucose $AUC_{0\text{-}24}$ increased 3.5% and C_{ave} increased 5.9% for the 5 mg QD group. For the 10 mg BID group, $AUC_{0\text{-}24}$ increased 1% and C_{ave} increased 16%. Coadministration of eplerenone with glyburide was well tolerated.
CONCLUSIONS: Coadministration of eplerenone 100 mg QD with glyburide did not have a clinically significant effect on insulin or glucose pharmacodynamic parameters. Eplerenone coadministration with glyburide did not clinically significantly alter the pharmacokinetics of glyburide and does not require dosage adjustment.

9. Effect of eplerenone on the anticoagulant activity of warfarin. *Susan E. Reid, M.Ed.,* Dwain S. Tolbert, Ph.D., James Ferry, Ph.D.; Pfizer Corporation, Skokie, IL; Takeda Pharmaceuticals, Lincolnshire, IL.

PURPOSE: Patients with cardiovascular disease normally require more than one medication to treat their disease state. This trial investigated the effect of eplerenone, a selective aldosterone blocker, on the pharmacokinetics of racemic warfarin and the effect of eplerenone on the anticoagulant activity of warfarin.
METHODS: Single-blind, randomized, two-sequence, placebo-controlled, parallel design trial in 25 healthy subjects. Subjects were titrated with warfarin (2-6 mg/day) to achieve prothrombin time (PT) values 1.2 to 1.7 times pretreatment values for 3 days and then received warfarin and eplerenone concomitantly.
RESULTS: Eplerenone coadministered with racemic warfarin did not statistically or clinically significantly change the mean PT values (p=0.7169). Comparison of Day 7 to Day 0 International Normalized Ratio (INR) values showed no significant differences for predose (p=0.4747) or 11 hours post-dose (p=0.0792). There were no significant differences between treatment groups regarding $AUC_{0\text{-}24}$, C_{max}, T_{max} or CL/F for total or free R-warfarin and S-warfarin. Coadministration of warfarin with eplerenone was safe and well tolerated.
CONCLUSIONS: Coadministration of eplerenone 100 mg QD with warfarin did not have a clinically significant effect on the anticoagulant activity of warfarin as measured by PT and INR. Steady-state eplerenone coadministration with warfarin did not significantly alter the pharmacokinetics of warfarin and does not require dosage adjustment.

10. Potential interaction between tenecteplase and unfractionated heparin in vitro. *James P. Tsikouris, Pharm.D.,* Christopher Martin, Pharm.D., Craig D. Cox, Pharm.D., Martin Ziska, B.S., Gary E. Meyerrose, M.D.; Texas Tech University, Lubbock, TX.

BACKGROUND: Tenecteplase (TNK), a thrombolytic for acute myocardial infarction, has displayed a lower risk of bleeding relative to other thrombolytic agents when combined with unfractionated heparin (UFH). Although many suggest the decreased bleeding is due to TNK's increased fibrin specificity, the potential for a drug-drug interaction with TNK lowering the pharmacologic propensity of UFH to cause anticoagulation and subsequent bleeding has not been explored.
METHODS AND RESULTS: In separate in vitro experiments exploring the relative influence of various thrombolytics with and without UFH on aPTT prolongation, we discovered a consistently surprising effect on aPTT prolongation when TNK and UFH were combined. In each of three separate experiments blood from 12 patients (n=36) was treated with different concentrations and combinations of thrombolytic agents and UFH. When comparing the effects of TNK + UFH versus UFH alone on aPTT prolongation, each study found a decrease in aPTT with the combination versus UFH alone (experiment 1: 137 ± 41 seconds vs. 187 ± 48 seconds, p=0.03; experiment 2: 59 ± 11 seconds vs. 75 ± 16 seconds, p=0.05; experiment 3: 59 ± 14 seconds vs. 78 ± 16 seconds, p=0.03). This contrasted the findings of other thrombolytic agents (alteplase and reteplase) combined with UFH, where aPTT was elevated versus UFH alone.
CONCLUSIONS: These findings indicate a possible drug-drug interaction between TNK and UFH, where TNK attenuates the intensity of anticoagulation with UFH in vitro, thus potentially explaining the reduced bleeding risk observed with the combination of TNK + UFH in acute myocardial infarction patients.

Cardiology

11. Exploring the effects of ACE inhibitor tissue penetration on vascular inflammation following acute myocardial infarction. *James P. Tsikouris, Pharm.D.,* Jose A. Suarez, M.D., Jan S. Simoni, Ph.D., Craig D. Cox, Pharm.D., Martin Ziska, B.S., Gary E. Meyerrose, M.D.; Texas Tech University, Lubbock, TX.

BACKGROUND: Questions remain as to the existence of a class effect amongst ACE inhibitors, and some literature suggests that pharmacologic effects and outcomes may be determined by an ACE inhibitor's propensity to penetrate and inhibit the ACE enzyme at the vascular tissue level. Because vascular inflammation contributes to adverse outcomes following acute myocardial infarction (AMI), and angiotensin II influences inflammation at the vascular level, we hypothesized that high-tissue penetrating ACE inhibitors would provide more favorable effects on C-reactive protein (CRP) after AMI compared to low-tissue penetrating ACE inhibitors.
METHODS AND RESULTS: In a randomized open-label trial, patients received the high-tissue penetrating quinapril (n=15) or low-tissue penetrating enalapril (n=15) following AMI. CRP was measured at baseline and periodically over 14 days following drug initiation. All baseline characteristics and blood pressure response to treatment between groups were equivalent. Prior to initiating study medication, CRP concentrations (mg/g) were similar between enalapril and quinapril (0.327 ± 0.348 vs 0.273 ± 0.154, respectively, p=0.77). The percent magnitude of change in CRP concentrations favored quinapril at all time points, starting 12 hours after treatment initiation. When characterizing CRP production during treatment, the time courses were significantly different and demonstrated lower CRP concentrations with quinapril (p=0.0107).
CONCLUSIONS: Overall, this investigation into the importance of ACE inhibitor tissue penetration on a common marker of vascular inflammation, suggests a potential vascular anti-inflammatory benefit with a more highly tissue penetrating ACE inhibitor following AMI. Further investigation into the true pharmacologic similarities and differences amongst this class of drugs is warranted.

12. Assessment of patient satisfaction with services provided by a clinical pharmacist managed cardiac risk reduction service. *Kari L. Olson, B.Sc., Pharm.D.,* Anne M. Denham, Pharm.D., Susan L. Holsclaw, Pharm.D., Roseanne Hornak, Pharm.D.; Kaiser Permanente, Denver, CO.

PURPOSE: Few studies have investigated patient satisfaction with clinical pharmacy services. Our Clinical Pharmacy Cardiac Risk Service (CPCRS) follows more than 9,000 patients with cardiovascular disease (CVD). Since its inception in 1998, no evaluation of patient satisfaction has been conducted. The purpose of this study was to determine the level of satisfaction among patients enrolled in CPCRS.
METHODS: A computer-generated, random list of 1,000 patients, enrolled in the service for at least 6 months, and had at least one contact by a clinical pharmacist were mailed a 21-question survey. The questions pertained to overall satisfaction and individual components of the service. A Likert-type scale was used for the majority of questions. Experts reviewed the survey for content and face validity. Analysis of results was primarily descriptive.
RESULTS: Of 1000 surveys mailed, 491 (49%) were returned. The average age of the population was 71.7 years, most were male (68.5%) and had been Kaiser Permanente members at least 5 years. The majority (83.7%) was satisfied with the care they received from CPCRS. Most (51.8%) felt the care was unique from that of other health care providers. Patients felt their clinical pharmacist was easy to contact (83.7%), provided timely service (94.8%), and addressed all questions/concerns in a way that was easy to understand (85.8%). Patients were content receiving care over the phone (86.8%) and by mail (90%), but were also willing to meet with the clinical pharmacist in person (70.8%).
CONCLUSIONS: Overall, patients indicated a high level of satisfaction with the services provided by clinical pharmacists at CPCRS.

13. What is the impact of physiologic increases in catecholamine concentrations on ventricular effective refractory period? *James S. Kalus, Pharm.D., BCPS,* Michael F. Caron, Pharm.D., Brian F. McBride, Pharm.D., Jeffrey Kluger, M.D., Danette Guertin, M.S.N., C. Michael White, Pharm.D.; University of Connecticut, Storrs, CT; Hartford Hospital, Hartford, CT; University of Rhode Island, Kingston, RI.

PURPOSE: Effective refractory period (ERP) is the period where cardiac myocytes are unable to accept depolarization stimuli and may represent a marker of arrhythmia vulnerability. β-blockers, may prevent arrhythmias by prolonging the ERP. Epinephrine reduces ERP, but the effect of norepinephrine on ERP in humans is unknown. Our objective was to assess the effect of physiologic doses of epinephrine and norepinephrine on ventricular ERP in patients with or without β-blockers (BBLs).
METHODS: ERP was measured in patients with implanted cardioverter-defibrillators who were undergoing defibrillation threshold testing. After testing, patients (n=50, 64.8 ± 13.1 years, 72% male, 70% CAD, EF = 35.8 ± 15.5%) were stratified by BBL use, then randomized to intravenous epinephrine, norepinephrine, or placebo (2 μg/min). After steady state was achieved (7 minutes), ERP measurement was repeated.
RESULTS: ERP was reduced 3.4% with epinephrine (p<0.001), while ERP

increased by 1.9% with norepinephrine infusion (p=0.029). Placebo had no effect. When the epinephrine and norepinephrine patients were analyzed by whether BBLs were used (n=20) or not (n=13), ERP was reduced in both epinephrine subgroups (BBLs: 3.2% reduction, p=0.003; No BBLs: 3.6% reduction, p=0.045). In the norepinephrine subgroups, only those taking BBLs experienced an increase in ERP (2.2% increase, p=0.013).
CONCLUSIONS: ERP is reduced by elevations in epinephrine concentrations regardless of beta-blocker therapy. This suggests that epinephrine could increase vulnerability to ventricular arrhythmias despite beta-blocker use, but norepinephrine does not.

14. An outcome evaluation of a pharmaceutical care service program to congestive heart failure patients. *Devada Singh, Pharm.D.,* Leanne Lai, Ph.D., Stan Hannah, Ph.D., Morton Diamond, M.D., Darla Erlich, ARNP, Maggie Gibbs, R.N., Deborah Wadsworth, ARNP; Nova Southeastern University; Broward General Medical Center, Fort Lauderdale, FL.

PURPOSE: To determine the impact of a pharmacist intervention program in an ambulatory CHF clinic.
METHODS: In this longitudinal, population-based study, a clinical pharmacist working in the CHF clinic alongside other medical clinicians evaluate patients' pharmacotherapy regimens, and make recommendations such as dosage adjustments, changing medications, and ordering labs. Educational materials, pillboxes, blood pressure kits and weight scales are distributed to enhance compliance. Clinical outcomes data are assessed 12-months pre- and post-intervention. Also, patients complete a quality of life – SF 12 questionnaire at baseline and at quarterly intervals.
RESULTS: In 25 patients, the mean age, weight and ejection fraction are 50.2 ± 10.3 years, 98.8 ± 31.5 kg, and 33.7 ± 14.6%, respectively. There were 106 interventions made. Ninety-six percent of patients had education on appropriate medication usage, 76% had education on lifestyle modifications, 56% required recommendation for laboratory testing, 32% received pillboxes, 28% had adjustment of doses, and 16% received weight scales. The paired t tests with 0.05 alpha level showed that the number of hospitalizations (p=0.014, 1.04 ± 0.98 vs 0.64 ± 0.81), and medications used (p=0.000, 6.64 ± 2.77 vs 8.72 ± 2.49) were significantly different after interventions. However, the number of signs and symptoms of CHF did not show significant difference (p=0.695, 2.6 ± 1.58 vs 2.76 ± 1.76).
CONCLUSIONS: Implementing a pharmaceutical care service program is associated with decreased hospitalizations of patients with congestive heart failure.

15. The association between activated clotting time and hemorrhagic complications in patients undergoing percutaneous coronary interventions with bivalirudin. *Estela M. Trimino, Pharm.D.,* Janelle M. Berg, Pharm.D., BCPS, Jose M. Martinez, MD, Manuel P. Anton, III, M.D.; Mercy Hospital, Miami, FL.

PURPOSE: To determine the correlation of ACT values to hemorrhagic complications with treatment of bivalirudin ± GPI during percutaneous coronary intervention (PCI).
METHODS: A retrospective, observational evaluation was conducted in 316 patients undergoing PCI with heparin ± GPI or bivalirudin ± GPI. High ACT values were defined as = 300 seconds and lower ACT values as < 300 seconds at end of procedure. Major bleeding included ≥ 3 gram drop in hemoglobin ± transfusion, or retroperitoneal, gastrointestinal, or intracerebral bleeds. Minor bleeding included oozing at sheath site, hematoma, and bleeding without need for transfusion. Major, minor, and total bleeds were compared to ACT groups and statistical analysis conducted.
RESULTS: Ninety-seven ACT values were obtained from 187 patients in the bivalirudin group, of which 53 (55%) were categorized as high. In the heparin group, fifty-four ACT values from 129 patients were obtained, and all were in the lower group. Ten major bleeds occurred in the bivalirudin group (5.3%; ACTs: 3 higher, 3 lower, 4 unknown) and 4 in the heparin group (3.1%; ACTs: 0 higher,1 lower, 3 unknown). Five of the ten major bleeds occurred with concomitant GPI in the bivalirudin group compared to three of four in the heparin group. Twenty-one bleeds (11%) were documented in the bivalirudin group and 23 (18%) in the heparin group (p=0.001), however the ACT value (higher versus lower) did not show significance (p=0.771).
CONCLUSIONS: Higher ACT values were not associated with increased bleeds in the bivalirudin group.

16. Differential regulation of mitogen activated protein kinases by angiotensin II receptor subtypes during myocardial ischemia-reperfusion injury. *Jeremy D. Flynn, Pharm.D.,* Ginell Post, M.D., Ph.D., Wendell S. Akers, Pharm.D., Ph.D.; University of Kentucky, Lexington, KY.

PURPOSE: Angiotensin subtype 1 receptor (AT1R) blockade reduces myocardial dysfunction and infarct size following myocardial ischemia-reperfusion injury. However, signaling pathways that contribute to the cardioprotective effects have not been identified. We hypothesized that the cardioprotective effects of AT1R blockade are associated with attenuating p38 and JNK activity and/or enhancing ERK activity.
METHODS: Rat hearts were perfused at a constant pressure and randomized to one of six treatments: time control (TC), vehicle (VEH), ischemic preconditioning (IPC; positive control), losartan (LOS; AT1R blocker), PD123319 (PD; AT2R blocker), or losartan/PD123319 (LOS/PD). Left ventricular end diastolic pressure (LVEDP) and developed pressure (LVDP) were monitored throughout the experimental protocol. Following 30 minutes of ischemia, hearts were reperfused for 30 minutes and immediately frozen for determination of MAPK activity by Western blot analysis. Gels were probed with specific antibodies that recognize total and phosphorylated forms of p38, ERK, and JNK. Results were expressed as the ratio of phosphorylated: total kinase levels (MAPK activity) and expressed relative to time control hearts. Data are reported as mean ± SD and were analyzed by ANOVA.
RESULTS:

Group	LV Function		MAPK Activity (phospo: total protein)		
(n=8/group)	LVEDP (mm Hg)	LVDP (mm Hg)	P38	JNK	ERK
TC	6 ± 2	116 ± 12	1.0	1.0	1.0
VEH	70 ± 19*	58 ± 15*	1.9 ± 1.3*	2.3 ± 1.1*	1.0 ± 0.5*
IPC	36 ± 11†	104 ± 18†	0.8 ± 0.6†	1.2 ± 0.9†	1.9 ± 0.7†
LOS	45 ± 14†	92 ± 11†	0.8 ± 0.6†	1.0 ± 0.4†	2.6 ± 1.0†
PD	58 ± 13	70 ± 15	2.3 ± 1.2	4.2 ± ±2.5	1.1 ± 0.3
LOS/PD	66 ± 13	74 ± 23	1.6 ± 1.2	3.4 ± 1.4	1.0 ± 0.9

*p<0.05 VEH vs TC; †p<0.05 IPC, LOS, PD, LOS/PD vs VEH

CONCLUSIONS: These data suggest that the cardioprotective effects of IPC and LOS are associated with attenuating p38/JNK and enhancing ERK activity. In addition, these data suggest the benefits of AT1R blockade may be partially mediated via unopposed AT2R stimulation.

17. Nitrous oxide sedation reduces discomfort caused by atrial defibrillation shocks. *Michael Ujhelyi, Pharm.D.,* Robert H. Hoyt, M.D., Kris Burns, R.N., Royce S. Fishman, Shailesh Musley, Ph.D., Michael H. Silverman, M.D.; Medtronic Inc., Minneapolis, MN.

Implantable cardioverter defibrillator with atrial therapies (ICD-AT) is an effective therapy to manage atrial tachyarrhythmias. Acceptance of this therapy, however, is limited by atrial shock-related anxiety and discomfort. Inhaled nitrous oxide (N_2O) is a potent sedative-analgesic-anxiolytic agent that may mitigate shock discomfort and anxiety, and improve patient ICD-AT acceptance. ICD-AT patients with >1 ambulatory atrial shock within12 months were enrolled and grouped by ICD-AT shock method; awake (awake method; n=9) or asleep (asleep method; n=4) when ambulatory ICD-AT shock is delivered. Baseline questionnaire assessed the most recent ambulatory ICD-AT shock (3 ± 3 months). A 65% N_2O/ 35% O_2 mixture was inhaled for 4 minutes followed by an ICD-AT test shock (18 ± 8 Joules). The test shock mimicked awake shock method. The test shock experience during N_2O was evaluated via questionnaire immediately following and 24 hours post-shock. Shock related anxiety, intensity, pain, and discomfort were assessed via 10-point rank scale. Baseline test shock scores were similar between shock method groups. In the awake shock method group, N_2O greatly reduced pre-shock anxiety by 48% (6.4 ± 2.4 to 3.3 ± 2.0, or), and shock related intensity (5.9±3.1 to 3.3 ± 2.5), pain (5.0 ± 2.6 to 2.0 ± 2.1), and discomfort (5.6 ± 2.4 to 1.3 ± 1.4) from baseline values by 45%, 60%, and 78% (p<0.05), respectively. The asleep shock method group reported no changes in shock related anxiety, intensity, pain or discomfort. Atrial shock concern, assessed via 5-point rank scale (5 = extreme concern) was improved by N_2O but only in the awake group (3.1 ± 1.0 baseline to 1.6 ± 0.5 N_2O, p=0.008). There were no adverse events with N_2O and patients fully recovered within 5 minutes after N_2O. Conclusions: 65% N_2O greatly reduced shock-related pain and discomfort, and significantly reduced atrial shock concern but only in the awake shock method group. The benefits of N_2O therapy may expand the use and acceptability of ICD-AT therapy into a larger AF cohort.

18E. Improving the acceptability of the atrial defibrillator: patient activated versus automatic night shocks with and without sedation. (The ADSAS 2 Study). Lana Boodhoo, MRCP, Andrew Mitchell, MRCP, *Michael R. Ujhelyi, Pharm.D.,* Neil Sulke, D.M., FRCP, FACC; Eastbourne General Hospital, Eastborne, United Kingdom; Medtronic Inc., Minneapolis, MN.

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19. Evaluation of practice patterns in a community hospital-based heart failure center: treating heart failure's special populations. *Jason M. Enders, Pharm.D., BCPS*; Paul P. Dobesh, Pharm.D., BCPS; St. Louis College of Pharmacy; St. Luke's Hospital, St. Louis, MO.

PURPOSE: Heart failure (HF) guidelines identify underserved patients (females and the elderly) not routinely receiving life-saving HF medications. We hypothesized that special populations are treated no differently in our ambulatory HF center. Our objective was to determine if medications with a mortality benefit in systolic HF [ACE-Inhibitors/ARBs, β-blockers (BB), spironolactone] are offered differently to special populations (males vs females, age < 70 years vs age ≥ 70 years) in our ambulatory HF center.
METHODS: A retrospective review of systolic HF patients in our ambulatory HF center was conducted for all patients enrolled as of 4/2003. Demographics, HF etiology, current HF medications, and HF hospitalizations between 4/2002-4/2003 were collected.

RESULTS: Data on 171 patients (63.7% male, mean age 70 ± 12 years) were collected. The overall rate of medication use was 98.1% for ACE-I/ARB, 79.2% for BB, and 35.6% for spironolactone. There was no significant difference in medication use between special populations.

	Male	Female	<70 years	≥70 years
ACE-I/ARB	99%	95%	98.6%	96.8%
BB	80%	77.8%	81.8%	78.4%
Spironolactone	33.9%	38.7%	32.4%	37%

Hospitalizations and total hospital days were not significantly different among the groups. Mean length of hospitalization was approximately three days longer for elderly females (7 days) compared to both young females and elderly males (p=NS).
CONCLUSIONS: Medications were offered equally to special populations treated in our ambulatory HF center. Optimal use of heart failure therapies in all patients may be attributed to pharmacist involvement in the disease-management model, in the development of treatment protocols, or combinations of these.

20. Implementation of a dofetilide order sheet in a community hospital setting. Mary Beth Bobek, Pharm.D., *Jennifer P. Askew, Pharm.D.*; New Hanover Health Network, Wilmington, NC.

PURPOSE: To simplify and improve compliance with Food and Drug Administration (FDA) recommendations for Tikosyn® (dofetilide) administration, an order sheet was developed and evaluated.
METHODS: A retrospective chart review was conducted on a total of 51 patient records, 26 records before and 25 after the institution of the order sheet. Patients were identified through the pharmacy computer for pre- and post-order sheet implementation. The order sheet was developed by a multidisciplinary team of cardiologists, pharmacists, and nurses. Before implementation of the order sheet, an education program was provided for physicians, nurses, and EKG technicians. Charts were reviewed pre- and post-implementation for the appropriateness of initial dosing, EKG orders, EKG administration time (2-3 hours post-dose), dose adjustments, baseline labs (K, Mg, SCr), daily labs (Mg, K), and the evaluation of drug interactions. One physician's patients were excluded due to a lack compliance with the mandatory monitoring.
RESULTS: Eighty percent of physicians used the dofetilide order sheet (n=20). EKGs were ordered according to FDA recommendations in 62% versus 92% of the population before and after the order sheet, respectively. EKGs were obtained in the recommended amount of time in 54% of the pre-order sheet group compared to 60% of the post-order sheet group. EKGs were performed without accordance to FDA recommendations or not at all in 35% of the pre-order sheet group and 12% of the post-order sheet group. More patients received baseline labs and recommended daily labs in the post-implementation group compared to the pre-implementation group (88% vs 42% and 83% vs 12%, respectively).
CONCLUSIONS: Implementation of a dofetilide order sheet and education program increases compliance with the recommended monitoring regimen for therapy initiation.

21. The effects of bupropion on autonomic response to mental stress. *Leslie A. Davidson, Pharm.D.,* Aliou D. Ousmanou, Pharm.D., Stan W. Carson, Pharm.D., Ralph Raasch, Pharm.D., Michael Golding, M.D.; University of North Carolina at Chapel Hill, Chapel Hill, NC.

PURPOSE: The chemical structure of bupropion is related to amphetamine, thus, it may have cardiovascular stimulatory properties. This study examined the effects of acute administration of bupropion on autonomic response in humans before, during, and after voluntary subjection to mental stress.
METHODS: Healthy, adult volunteers were eligible for this double-blind, crossover, placebo-controlled, single-center pilot study. Subjects were randomized to receive sustained-release bupropion titrated to 150 mg twice daily over 7 days, or corresponding placebo, with a three day wash-out period between treatments. After each treatment period, each subject underwent a 2-hour clinic visit, where separate speech and math "stress" tests were administered. Heart rate was recorded every minute, and plasma catecholamines were measured before, during and after each stress test.
RESULTS: Twelve subjects participated in this study. Average heart rates were significantly higher after bupropion versus placebo 30 minutes prior to speech test administration (74 vs 65, p<0.0003), while subjects listened to their recorded speech, (83 vs 73, p<0.008), and 15 minutes after speech and math tests (81 vs 75, p<0.007). Plasma norepinephrine serum levels were significantly higher in subjects after taking bupropion versus placebo during speech test administration, (260 ± 100 vs 207 ± 124 pg/ml, p<0.03).
CONCLUSIONS: Autonomic response to mental stress was greater after treatment with bupropion for 7 days than placebo. These alterations in heart rate and plasma norepinephrine levels may be detrimental in patients at increased risk for cardiovascular disease. Further studies are necessary to establish definitive effects of bupropion on hemodynamic variables and the potential clinical consequences.

22. Variability in serum digoxin concentrations in the Digitalis Investigational Group trial: a retrospective analysis. *Craig R. Lee, Pharm.D.,* Pinal J. Shah, Pharm.D., Kirkwood F. Adams, Jr., M.D., Wendy A. Gattis, Pharm.D., Christopher M. O'Connor, M.D., Mihai Gheorghiade, M.D., Todd A. Schwartz, M.S., J. Herbert Patterson, Pharm.D., FCCP; University of North Carolina, Chapel Hill, NC; Duke University, Durham, NC; Northwestern University, Chicago, IL.

PURPOSE: Recent retrospective analyses suggest that low serum digoxin concentrations (SDCs) (0.5–0.9ng/ml) may be associated with improved survival in patients with left ventricular dysfunction, while higher concentrations (≥1.2ng/ml) within the traditional therapeutic range appear harmful. However, dosing strategies that achieve optimal SDCs remain to be defined.
METHODS: To characterize the expected dose-SDC relationship in heart failure patients, we performed a retrospective, frequency distribution analysis of 1575 patients enrolled in the Digitalis Investigational Group (DIG) trial randomized to digoxin with a blinded, 4-week SDC determined 6-30 hours after dosing. Initial doses were determined by a standard nomogram accounting for age, gender, weight, renal function, and concomitant medications.
RESULTS: Digoxin doses of 0.125, 0.25, and 0.375 mg/day were administered to 18%, 72%, and 9% of patients, respectively. Across all doses, the median ± interquartile range SDC was 0.80 ± 0.50 ng/ml, with 8%, 53%, 24%, and 3% having SDCs <0.5 (undetectable), 0.5–0.9, ≥1.2, and ≥2.0 ng/ml, respectively. Despite the nomogram, patients receiving 0.125mg/day had lower median SDCs compared to 0.25mg/day (0.7 vs 0.9 ng/ml, p<0.001), more undetectable SDCs (15% vs 7%, p<0.001), and fewer supratherapeutic SDCs (≥1.2ng/ml: 15% vs 26%, p<0.001; ≥2.0ng/ml: 1% vs 3%, p=0.045), respectively. The proportion of therapeutic SDCs (0.5–0.9ng/ml) was similar across doses (53% vs 53%, p=0.888).
CONCLUSIONS: In the DIG trial, optimal SDCs were obtained on average by dosing according to a standard nomogram; however, substantial variability still existed at all doses. Although SDCs ≥2.0ng/ml were minimized, reevaluation of this dosing strategy may be necessary to reduce the occurrence of SDCs ≥1.2ng/ml.

23E. Favorable effects of digoxin on morbidity and mortality in patients with class IV CHF due do systolic dysfunction: retrospective analysis of the Digitalis Investigational Group trial. *Pinal J. Shah, Pharm.D.,* Craig R. Lee, Pharm.D., Kirkwood F. Adams, Jr. M.D., Wendy A. Gattis, Pharm.D., Christopher M. O'Connor, M.D., Mihai Gheorghiade, M.D., Todd A. Schwartz, M.S., J. Herbert Patterson, Pharm.D., FCCP, BCPS; University of North Carolina, Chapel Hill, NC; Duke University Medical Center, Durham, NC; Northwestern University, Chicago, IL.

Presented at the 52nd Annual Scientific Session of the American College of Cardiology, Chicago, IL, March 31, 2003.

24. Influence of gender on the aggressiveness of titrating essential medications for chronic heart failure. *Tien M.H. Ng, Pharm.D.,* Chris N. Kotschwar, Katie M. Groen , Julie A. Stoner, Ph.D., Tom D. Sears, M.D.; University of Nebraska Medical Center, Omaha, NE.

PURPOSE: Studies suggest the management of cardiovascular disease and heart failure (HF) is suboptimal for women. The objective of this pilot study was to examine whether the dosing of life-prolonging HF medications, specifically angiotensin converting enzyme inhibitors (ACE-I) and β-adrenergic antagonists (BB), is less aggressive for women than men.
METHODS: In a retrospective, cohort design, consecutive HF patient charts (identified by ICD-9 coding) from January 1, 1999 to December 31, 2001 were screened from the university database. Inclusion criteria were HF diagnosis after Jan 1, 1996, left ventricular ejection fraction (LVEF) #40% and age $40 years. Prescribing data for ACE-I and BB were collected and included generic name of agent, initial dose and initiation date, subsequent clinic visits and dosage titrations dates, and corresponding cardiac vital signs.
RESULTS: Fifty-nine charts met inclusion criteria (21 females, 38 males). Male (M) and female (F) cohorts were of similar age, race, HF etiology, functional classification, and LVEF. Mean (standard deviation) time for up-titration (M 32.0 ± 42.4 vs F 47.1 ± 47.5 days, p=0.004) and the percentage requiring more than 1 visit for an up-titration (M 16% vs F 33%, p=0.01) of ACE-I were significantly greater for females in a multivariate regression model. No differences were detected for BB. Mean final maintenance doses of ACE-I and BB, maintenance systolic blood pressure and heart rate were not different between groups. Mean maintenance diastolic blood pressure was significantly lower for females (M 73.6 ± 12.6 vs F 65.3 ± 11.3 mm Hg, p=0.01).
CONCLUSIONS: Female gender was associated with less aggressive up-titration of ACE-I, but not BB. However, maintenance targets were similar regardless of gender. Continued efforts to increase awareness regarding the management of cardiac disorders and to investigate methods for improving care of female cardiovascular patients are needed.

25E. The adherence to a postoperative atrial fibrillation protocol in cardiothoracic surgery patients. *Robert A. Barcelona, Pharm.D.,* Kerry K. Pickworth, Pharm.D.; Ohio State University Medical Center, Columbus, OH.

Presented at the Great Lakes Residency Conference, Indianapolis, IN, May 2003.

26. Oral sedation improves patient perception of shock delivery with an implantable atrial defibrillator. *Tanya J. Fabian, Pharm.D.,* Michael R. Ujhelyi, Pharm.D., David S. Schwartzman, M.D., Kristin L. Bigos, B.S., Sharon E. Corey, Ph.D., Patricia D. Kroboth, Ph.D.; University of Pittsburgh, Pittsburgh, PA; Medtronic Inc., Minneapolis, MN.

PURPOSE: Intra-atrial shock therapy delivered via an implanted atrial defibrillator (IAD) is highly efficacious in the termination of atrial fibrillation (AF) in patients with symptomatic, drug-refractory atrial arrhythmias. Patient acceptance of this therapy, however, is limited by atrial shock-related anxiety and discomfort. Therefore, we evaluated the effect of sedation therapy on patient perception of shock delivery and memory for therapy with an IAD.
METHODS: Fifteen patients (11 men, 4 women; mean age: 59 ± 9 years) participated in this balanced, double-blind, crossover study of oral triazolam (0.375 mg) and placebo. Atrial shock was administered approximately 75 minutes after drug ingestion, and all patients were conscious at the time of shock. Patients rated shock discomfort immediately after shock. Approximately 12 hours later, patients rated pre-shock anxiety, and shock pain, discomfort and intensity.
RESULTS: Eighty percent of patients preferred pre-medication with triazolam versus placebo. Triazolam significantly reduced pre-shock anxiety and shock-related pain and intensity relative to placebo by 34%, 33%, and 29%, respectively; all $p<0.05$. Patients also recalled less shock discomfort the morning after shock delivery with triazolam. Throughout the study, sedation scores were ≤ 3 (0=no sedation, 4=extreme sedation).
CONCLUSIONS: In these anxious patients, triazolam produced mild sedation, which resulted in a significant reduction in pre-shock anxiety, shock pain and intensity. Patients recalled less discomfort with triazolam than placebo suggesting that adjunctive sedation altered the memory of the shock experience. These data indicate that oral triazolam improves patient perception of the IAD shock experience and may ultimately enhance acceptance of this therapy.

27. The pharmacokinetics of eplerenone in patients with left ventricular dysfunction/heart failure. Susan E. Reid, M.Ed., Matthew M. Hutmacher, M.S., Dwain S. Tolbert, Ph.D., James Ferry, Ph.D.; Pfizer Corporation, Skokie, IL; Takeda Pharmaceuticals, Lincolnshire, IL.

PURPOSE: Aldosterone plays a major role in extracellular fluid volume expansion in heart failure (HF) patients. Therefore, the effect of HF on the population pharmacokinetics of eplerenone, a selective aldosterone blocker (SAB), was evaluated in adult patients with left ventricular dysfunction/HF.
METHODS: The Eplerenone Post-AMI Heart Failure Efficacy and Survival Study (EPHESUS) was a multicenter, randomized, double-blind, placebo-controlled, 2-arm, parallel-group study designed to evaluate the effect of eplerenone on morbidity and mortality in patients with acute myocardial infarction with HF and left ventricular dysfunction who were receiving standard therapy. Sparse blood sampling techniques were utilized to determine the population pharmacokinetics of eplerenone. A total of 258 patients were enrolled in this population pharmacokinetic sub-study, with 134 patients receiving eplerenone.
RESULTS: A one-compartment model with first-order absorption adequately characterized the pharmacokinetic profile of eplerenone following oral dosing. The population mean estimate of plasma clearance (CL/F) reported in this trial for HF patients (4.91 L/hour) is less than that determined in young healthy volunteers (9.63 L/hour), but is similar to elderly healthy volunteers (6.60 L/hour) and to the reported CL/F in a 5-day multiple dose pharmacokinetics trial in patients diagnosed with HF (New York Heart Association Class II-IV) (5.36 L/hour). No covariates were found to influence CL/F.
CONCLUSIONS: The population mean estimate of CL/F reported in HF patients is similar to that of healthy volunteers of comparable age.

28. Depression is associated with adverse outcomes in patients with decompensated heart failure. *Simon de Denus, M.S.,* Sarah A. Spinler, Pharm.D., Mariell Jessup, M.D., Andrew Kao, M.D.; University of the Sciences in Philadelphia; University of Pennsylvania, Philadelphia, PA.

PURPOSE: Depressed with heart failure (HF) have higher long-term mortality and re-hospitalization rates compared to patients without depression. The impact of depression on patients with decompensated HF is unknown.
METHODS: Observational single center study of consecutive patients hospitalized with decompensated HF included in the Acute Decompensated Heart Failure Registry (ADHERE) admitted in the coronary care unit and the cardiac intermediate care unit of a tertiary referral center. The impact of a prior history of depression on the combined end point of in-hospital death, discharge to hospice or cardiopulmonary resuscitation was assessed.
RESULTS: Of the 182 patients with a first ADHERE hospitalization, 11 were excluded because they underwent cardiac transplantation during the hospitalization. A total of 171 patients were included. Sixty-four percent were male, 63% were Caucasians, 84% had a prior history of HF, 57% had a history of coronary artery disease and the mean LVEF prior to hospitalization was 27.4%. Patients with a prior history of depression (n=34) tended to have a higher likelihood of experiencing the combined end point as compared to patients without depression (n=137) (17.6% vs 7.3%; Fisher Exact, p=0.09). A multivariate regression analysis was performed to adjust for baseline demographics, prior medical history, medications and baseline laboratory values. Depression was significantly predictive of the combined end point (OR = 4.2 95% CI: 1.1-15.8; $p<0.04$).
CONCLUSIONS: Our study suggests that depression is associated with an increased risk of in-hospital adverse outcomes in patients with decompensated HF.

29. Rate control versus rhythm control in patients with atrial fibrillation: a meta-analysis. *Simon de Denus, M.S.,* Cynthia A. Sanoski, Pharm.D., Sarah A. Spinler, Pharm.D.; University of the Sciences in Philadelphia; University of Pennsylvania, Philadelphia, PA.

PURPOSE: For many clinicians, the primary treatment strategy for patients with atrial fibrillation (AF) is reestablishing and maintaining sinus rhythm (rhythm control), although the data supporting this approach over a rate control and anticoagulation strategy is not available. Furthermore, recent trials showed no difference in the risk of mortality between the two strategies. This could be secondary to insufficient sample sizes. We performed a meta-analysis of trials comparing the effects of these two strategies on the risk of all-cause mortality.
METHODS: We conducted a meta-analysis of randomized trials comparing rhythm control and rate control strategies in patients with AF. A literature search of published English language clinical trials was performed in Medline (1966 to June 2003), the Cochrane Controlled Trials Registry (First quarter 2003) and International Pharmaceutical Abstracts (1970 to May 2003). Trials of postoperative AF were excluded.
RESULTS: Four trials were included (AFFIRM, RACE, PIAF, STAF). The overall mortality rate was similar between patients in the rate control and rhythm control strategies (rate control: 3.7% vs rhythm control: 4.0%; OR: 0.87, 95% CI: 0.75-1.02; $p=0.10$).
CONCLUSIONS: A rhythm control strategy is not associated with a reduction of all-cause mortality in patients with AF as compared to a rate control strategy. Although a rhythm control strategy may be a valuable strategy in selected patients, it may not be the preferred strategy in all patients with AF.

30. Appropriate treatment of systolic heart failure in the primary care clinics. *Thomas J. Worrall, B.S.,* Kit N. Simpson, Dr.PH., Dorothy E. Jenrette, Pharm.D., BCPS; Ralph H. Johnson VA Medical Center; Medical University of South Carolina, Charleston, SC.

PURPOSE: Heart failure is a common medical condition affecting over five million people in the United States. Many experts believe that suboptimal pharmacological treatment contributes significantly to hospitalizations and deaths. This study was designed to quantify the percentage of patients in the primary care clinics receiving appropriate therapy for systolic heart failure (SHF) and to potentially improve prescribing practices in this patient population.
METHODS: Male veterans with SHF [defined as an ejection fraction (EF) < 40%] from three primary care teams were evaluated. Patients with SHF were randomly selected from the fourth quarter of 2001. The primary endpoints evaluated were the percentage of patients on angiotensin converting enzyme inhibitor (ACEI), β-adrenergic receptor antagonist (β-blocker), or combination therapy. The secondary endpoint evaluated was the percentage of patients on spironolactone. Following the initial retrospective chart review, two educational interventions were performed in April and June 2002 to increase compliance with the SHF treatment guidelines. The effectiveness of this education was assessed through a review of SHF patient charts from the third quarter of 2002 using the same methods described in the initial retrospective evaluation. Logistic regression modeling was used to assess the effect of the educational interventions. The Likelihood Ratio was used to assess overall model significance, and each variable was assessed using chi-square. The Wald Confidence Interval (CI) for the odds ratio estimates was also calculated.
RESULTS: A total of 148 patients were evaluated (75 pre- and 73 post-education). The mean age of the patients was 65 years ± 11.3 years, the mean EF was 29% ± 9.5%, and the mean number of drugs prescribed per patient (other than study drugs) was 9.5 ± 4.8. The New York Heart Association (NYHA) functional class distribution was similar between groups. The percentages of patients prescribed ACEI in the pre- and post-education groups were 90.7% and 89%, respectively. In the post-education group, there was a 12.8% increase in β-blocker prescribing and a 6.2% increase in spironolactone prescribing. Spironolactone prescribing increased 10% in NYHA class III and IV heart failure patients. These patients were also 3.7 times more likely to receive appropriate therapy (95% CI 1.16-11.63, p = 0.026).
CONCLUSIONS: These results indicate that pharmacists' educational interventions significantly improved the appropriate pharmacological treatment of SHF in the primary care clinics.

31. Acute coronary syndromes: quality of care in an academic VA medical center. *Nicole L. McMaster, Pharm.D.,* Sharon A. Jung, Pharm.D., Thane C. Erwin, R.Ph., William D. Linn, Pharm.D.; South Texas Veterans Health Care System, San Antonio, TX.

PURPOSE: This study documents quality of care received by veterans admitted with an acute coronary syndrome (ACS) specifically assessing patients who did not receive angiography, and percent of patients discharged on appropriate oral medications as defined by current guidelines.
METHODS: There were 30 patients admitted between October 1 and December 31, 2002 with an ACS who met entry criteria. Fifty-four patients were excluded. The American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for Cardiac Catheterization were used to evaluate eligibility for angiography. ACC/AHA Acute Myocardial Infarction Guidelines were used to determine appropriate discharge medications. Patients' hospital course, invasive and non-invasive procedures, and discharge medications were documented.
RESULTS: Cardiac catheterization occurred in 20 patients. Of the 10 not catheterized, 3 refused, 6 did not have an indication or had a contraindication, and 1 had an outpatient cath scheduled. Of the 20 patients catheterized, 12 underwent percutaneous coronary intervention (PCI) with 6 receiving coronary stents. Appropriate discharge medications included antiplatelet agents (100%), β-blockers (97%), angiotensin converting enzyme inhibitors (97%), and HMG co-A reductase inhibitors (87%).
CONCLUSIONS: Recently published data implied the underuse of angiography in the Veterans Affairs (VA) Health Care System as compared to a fee-for-service system. These data were for patients discharged from 1994 to 1995. Our data indicate that all patients with an indication for angiography received the procedure unless contraindicated or refused. There did not appear to be an underuse of PCI or stenting. Additionally, appropriate discharge medications were given to a vast majority of patients.

32. Evaluation of lipid management following coronary artery bypass graft surgery. *Angela R. Lumpkin, Pharm.D.,* J. Wayne Hamm, Pharm.D., Katherine C. Herndon, Pharm.D., BCPS; Birmingham Veterans Affairs Medical Center; Pfizer Inc., Birmingham, AL.

PURPOSE: This review was designed to assess the lipid management of patients who underwent coronary artery bypass graft (CABG) surgery at a Veterans Affairs Medical Center.
METHODS: A medical record review was conducted in 63 patients who underwent CABG surgery at the Birmingham VA Medical Center between September 1, 2001 and February 28, 2002. Patient demographics, medical history, type and number of bypass grafts, and lipid profiles (within 12 months prior to CABG) were documented. Lipid-lowering drug therapy was documented upon admission for surgery and up to 90 days following hospital discharge.
RESULTS: The mean age of the patient population (95.2% male) was 62.4 years. The mean number of grafts was 3.2, and one or more saphenous vein grafts were used in 62 patients (98.4%). Prior to CABG surgery, the mean LDL cholesterol was 102.8 mg/dL (n=40), and 20 patients (31.7%) had achieved the goal LDL cholesterol of <100 mg/dL. Lipid-lowering therapy was documented in 36 patients upon admission for surgery, but only 16 patients at discharge (admission lipid-lowering therapy was discontinued in 22 patients). Lipid-lowering therapy was initiated/restarted in five patients at the first follow-up visit (mean time to follow-up = 13.8 days), and 12 patients within 90 days of discharge. Thus, 33 of 60 patients (3 documented deaths) were receiving lipid-lowering therapy within 90 days of discharge following CABG surgery.
CONCLUSIONS: Despite numerous clinical trials demonstrating the beneficial effects of lipid-lowering therapy on angiographic and clinical outcomes, lipid management is often overlooked in the post-CABG setting.

33. Cardiac restitution predicts the effects of dofetilide on arrhythmogenesis. *J. Jason Sims, Pharm.D.,* Jennifer M. Loeb, B.S., Nicholas A. Wiegert, B.S., Robert M. Twieg; University of Wisconsin, Madison, WI.

PURPOSE: The cardiac restitution hypothesis states that a steeply sloped restitution curve, relationship between the action potential duration (APD) on the previous diastolic interval (DI), creates unstable wave-front propagation resulting in wave break and ventricular fibrillation (VF). Further, it has been shown that antiarrhythmic drugs with multiple ion channel effects reduce cardiac restitution curve slope and prevent VF. However, we have previously shown that cardiac restitution does not correctly predict the effects of singular sodium channel blockade on arrhythmogenesis. Thus, the current study assesses the effects of singular potassium channel blockade on arrhythmogenesis.
METHODS: Cardiac restitution curves were constructed from intact swine hearts using a combination pacing and monophasic action potential probe placed at the left ventricular lateral wall endocardium. The heart was paced for 50 beats at cycle lengths ranging from 400 ms to 180ms. Exponential fit restitution curves were constructed from the last beat APD90 (y-axis) versus the preceding DI (x-axis) during baseline and during intravenous placebo (n=8) or dofetilide 6 mg/kg/hour (n=7).
RESULTS: Dofetilide significantly decreased the average restitution curve slope (see table, *p=0.02 vs baseline). Importantly, the number of VF episodes during restitution testing at baseline was 0.4 + 0.3 versus 0.5 + 0.2 for dofetilide. There were no changes in any parameter during placebo.

Baseline	Dofetilide	Baseline	Placebo
1.9±0.3	1.1±0.1*	1.6±0.2	1.5±0.3

CONCLUSIONS: It is hypothesized that decreasing cardiac restitution slope explains antiarrhythmic drug activity. The current study indicates that dofetilide decreases the cardiac restitution slope and did not increase arrhythmogenesis. Thus, it appears that the cardiac restitution hypothesis correctly predicts the effects of antiarrhythmic drugs with singular potassium channel blockade. Based on our previous results it may be that the predictive ability of cardiac restitution is ion channel specific.

Critical Care

34. The green tea polyphenol epigallocatechin gallate attenuates interferon-GAMMA induced hyperpermeability in cultured human intestinal monolayers. *David R. Foster, Pharm.D.,* Brian R. Overholser, Pharm.D.; Purdue University, Indianapolis, IN.

PURPOSE: Intestinal barrier integrity is diminished in critical illness, leading to permeation of inflammatory stimuli and translocation of enteric bacteria. Inflammatory cytokines, including interferon-γ (IFN), play an important role in mediating intestinal dysfunction. Epigallocatechin gallate (EGCG) is a naturally occurring polyphenol derived from green tea with potent antioxidant and anti-inflammatory properties. We hypothesized that EGCG would prevent IFN-mediated hyperpermeability in cultured human intestinal monolayers (Caco-2 cells).
METHODS: Caco-2 monolayers were grown on permeable supports. Treated cultures were incubated in triplicate with combinations of IFN (50 ng/ml) and EGCG (10 and 100 µmol) for 72 hours. Monolayer integrity was assessed before and after IFN/EGCG treatment by measuring the transepithelial electrical resistance (TEER) of the monolayers using an epithelial volt-ohmmeter.
RESULTS: IFN treatment caused a profound decrease in TEER that was partially attenuated by EGCG 100 µmol, but not EGCG 10 µmol (table). Post-hoc analyses (Wilcoxin rank sum test) confirmed that the reduction in TEER was lower in cultures treated with EGCG 100 µmol +IFN than those treated with IFN alone ($p<0.05$) and EGCG 10 µmol +IFN ($p<0.05$).

	Control	IFN	EGCG 10 µmol	EGCG 100 µmol	EGCG 10 µmol +IFN	EGCG 100 µmol +IFN	p*
TEER†	-14.9 (-7.7, -22.1)	-57.3 (-54.3, -67.9)	-19.5 (-12.9, -26.0)	-10.8 (-8.1, -12.5)	-59.8 (-59.3, -63.0)	-34.8 (-31.1, -34.9)	0.01

† median % change from baseline (range); * Kruskal-Wallis

CONCLUSIONS: EGCG 100 µmol attenuates IFN-induced reductions in Caco-2 monolayer integrity. These findings imply that polyphenolic compounds found in green tea may prevent intestinal hyperpermeability during critical illness. Future efforts should be directed at determining the clinical implications of these findings.

35E. Association of red blood cell transfusions and hemoglobin on intensive care unit length of stay. *Samir H. Mody, Pharm.D., M.B.A.,* Kathleen M. Kelly, M.D., FACS, FCCM, Patrick Lefebvre, M.B.A., BEE, Mei Sheng Duh, M.P.H., Sc.D.; Ortho Biotech Products L.P., Bridgewater, NJ; Ortho Biotech Products, L.P., Bridgewater, NJ; Analysis Group, Montreal, PQ, Canada; Analysis Group, Boston, MA.

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36. Evaluation of hypotension and its relationship to volume status in patients receiving dexmedetomidine. *Anthony T. Gerlach. Pharm.D.,* Joseph F. Dasta, M.Sc.; Ohio State University Medical Center, Columbus, OH.

PURPOSE: Dexmedetomidine (DEX) is a novel sedative approved for use in critically ill patients, and is associated with hypotension and bradycardia. A prospective medication use evaluation revealed hypotension occurred in 48% of patients at our institution. The purpose of this study is to evaluate the association of hypotension from DEX and intravascular volume status.
METHODS: Data collected retrospectively on any patient receiving DEX in the surgical ICU included: demographics, indication, dosing, length of therapy, adverse effects, and central venous pressure (CVP). Hypotension was defined as systolic blood pressure less than 90 mm Hg or mean blood pressure less than 60 mm Hg. Hypovolemia was defined as a CVP less than 12 mm Hg. Statistics were preformed by Fisher's Exact Test.
RESULTS: Twenty-seven patients received DEX from 12/01 to 5/03. The mean maximum dose of DEX was 0.51 µg/kg/hour (range 0.05-0.7 µg/kg/hr), and administered for a mean of 19.8 hours. Only 4 patients received a loading dose. Hypotension occurred in 13 patients (48%) including 3 patients who needed vasopressors. CVP was transduced in 15 patients, and 10 of these developed hypotension. Seven of 9 patients (78%) developed hypotension

with a CVP less than 12 mm Hg, and 3 of 6 patients (50%) developed hypotension with a CVP greater than or equal to 12 mm Hg (p=0.33).
CONCLUSIONS: Dexmedetomidine was dosed according to manufacturer recommendations. The incidence of hypotension does not seem to be associated with intravascular volume status in patients receiving DEX. Refined patient selection may minimize the incidence of hypotension associated with DEX.

37E. Evaluation of drotrecogin alfa treatment guidelines. *Jeffrey P. Gonzales, Pharm.D.,* Lori L. Siatkosky, Pharm.D., Jennifer K. Long, Pharm.D.; Cleveland Clinic Foundation, Cleveland, OH.

Published in Crit Care Med. 2003;30(12):A454.

38E. Experience with drotrecogin alfa activated in an urban tertiary care medical center. *Eric Wittbrodt, Pharm.D.,* Christina Rose, Pharm.D., Paul Birnbaum, M.D., Avelino Verceles, M.D., Herbert Patrick, M.D.; Philadelphia College of Pharmacy; Hahnemann University Hospital; Drexel University, Philadelphia, PA.

Published in Crit Care Med 2002;30:A104.

39E. A comparison of the bispectral EEG and Hahnemann Sedation Assessment Scale. *Eric Wittbrodt, Pharm.D.,* Christina Rose, Pharm.D., Herbert Patrick, M.D.; Philadelphia College of Pharmacy; Drexel University, Philadelphia, PA.

Published in Crit Care Med 2002;30:A158.

Drug Delivery

40. Bioequivalence of the oral direct thrombin inhibitor ximelagatran when administered as a crushed tablet with applesauce or via nasogastric tube. *Kajs-Marie Schützer, M.D., Ph.D.,* Carina E. Lonnerstedt, B.M.S., Ulrica E. Wall, M.D., Ph.D., Lis M. Ohlsson, M.Sc., Troy C. Sarich, Ph.D., Renli Teng, Ph.D., Ulf G Eriksson, Ph.D.; AstraZeneca R&D Molndal, Molndal, Sweden; AstraZeneca LP, Wilmington, DE.

PURPOSE: To investigate whether 2 alternative routes of gastrointestinal administration affect the pharmacokinetic profile of ximelagatran (Exanta(TM), AstraZeneca). Ximelagatran is currently under development for the prevention and treatment of thromboembolic disorders.
METHODS: In an open, randomized, 3-period, 3-treatment, crossover study, healthy volunteers (n=40; aged 20-50 years) received 3 treatments of a single 36-mg, immediate-release ximelagatran tablet, in an order determined by randomization, on 3 study days separated by washout periods of 2 to 14 days. Tablets were: A) swallowed whole, B) crushed, mixed with applesauce, and ingested, and C) dissolved in water and administered via nasogastric tube. Plasma concentrations of melagatran, the active form of ximelagatran, were measured for determination of AUC and C_{max} values.
RESULTS: Thirty-nine volunteers completed the study (n = 38 for treatment 3). The least-squares estimates (with 94% CI) of the between-treatment ratios (treatment B: treatment A and treatment C: treatment A) for AUC were 1.01 (0.965-1.06) and 0.970 (0.924-1.02), respectively; and for C_{max} were 1.04 (0.972-1.11) and 1.02 (0.955-1.10), respectively. These ratios and their CIs were within the 94% CI predefined to demonstrate no pharmacokinetic interaction (0.80-1.25). The plasma T_{max} of melagatran (~ 2 hours) did not vary significantly with administration route. Ximelagatran was well tolerated, and tolerability was unaffected by administration route.
CONCLUSIONS: The pharmacokinetics of the oral DTI ximelagatran as an immediate-release tablet were not significantly altered whether crushed and mixed with applesauce and given orally, or dissolved in water and given via nasogastric tube.

41. Rapid infusion of a novel IVIG preparation liquid-formulated with glycine (IGIV-C; Gamunex™, 10%). *John Strell, R.Ph.,* Kim Hanna, M.S., the IGIV-C in ITP Study Group; Bayer HealthCare, West Haven, CT; Bayer HealthCare, Research Triangle Park, NC.

Since the introduction of intravenous immunoglobulin (IVIG) into clinical practice, dosing has escalated (typically 1000-2000 mg/kg, over 1-2days), as higher doses have been associated with increased clinical benefit. Higher IVIG doses, however, evoke concerns of excessive time required for infusion to avoid adverse events (AEs), fluid volume overload, and hyperosmolality issues associated with sugar formulations. Infusion rates are conservative based on manufacturers' recommendations (typical range, 0.02-0.08 ml/kg/minute or 2-8 mg/kg/minute for 10% solution) to minimize AEs.
PURPOSE: The current study investigated tolerability of increased infusion rates of a novel IVIG liquid-formulated with glycine (IGIV-C; Gamunex(TM), 10%).
METHODS: This unblinded, randomized, multicenter study in patients with chronic idiopathic thrombocytopenia did not permit pre-medication with corticosteroids to reduce or relieve potential AEs. A randomized sequence of 3 infusion rates was administered to patients (n=21), each initiated at 0.01ml/kg/min, increased to 0.08ml/kg/minute within 30 min, and adjusted to the final target rate (0.08, 0.11, or 0.14 ml/kg/min) within 30 minutes if no AEs occurred. Doses (~1000mg/infusion) were administered every 4-6 weeks.
RESULTS: Drug-related AEs occurred in 23-36% of patients. The only drug-related AE occurring in ≥10% of patients in any group was headache (4-23%; all rated "mild"). No thromboses or adverse effects on renal function were observed.
CONCLUSIONS: These data indicate that the increased IGIV-C infusion rates studied here do not influence severity or incidence of AEs. Estimating total IGIV-C infusion time with inclusion of initial rate ramp up, doses of 1000 and 2000 mg/kg could be completed in <2 and ~3 hours, respectively.

42. The pharmacokinetics and bioavailability of metoclopramide and naproxen from MT 100™ tablets. *Susan E. Spruill, M.S.,* William Wargin, B.S.Pharm., Ph.D., Diane Littlefield, R.N., M.S.N., John R. Plachetka, Pharm.D.; POZEN® Inc., Chapel Hill, NC.

PURPOSE: MT 100(TM) is a novel combination product of metoclopramide hydrochloride and naproxen sodium intended for treatment of acute migraine attacks. MT 100 is a unique tablet design that releases metoclopramide hydrochloride followed by naproxen sodium in a coordinated and sequential manner. The purpose of this study was to evaluate the pharmacokinetics and bioavailability of metoclopramide and naproxen from MT 100 tablets (one and two tablets) compared with metoclopramide and naproxen administered as individual components.
METHODS: This was a Phase I, randomized, four-period crossover, single-dose pharmacokinetic study in 24 healthy volunteers. All study doses were administered under fasting conditions and were separated by at least a 5-day washout period. Blood samples were obtained over a 72-hour time period and plasma was analyzed using validated HPLC methods.
RESULTS: The mean and median naproxen t_{max} values for MT 100 were both significantly earlier than for naproxen alone (means of 44 vs 72 minutes and medians of 40 vs 50 minutes, respectively) with a difference of more than 180 minutes (3 hours) in 2 subjects. The 90% confidence intervals around the ratios of least-squares means for the ln-transformed parameters AUC_{last}, AUC_{∞} and C_{max} for naproxen and metoclopramide were within the 80-125% FDA acceptance range for bioequivalence.
CONCLUSIONS: The combination of metoclopramide and naproxen in the MT 100 formulation produced a significantly earlier t_{max} for naproxen compared to the administration of naproxen alone. Also, the AUC and C_{max} values for metoclopramide and naproxen for the MT 100 formulation versus the individual components were of similar magnitude. The safety profiles of MT 100 and the individual components were similar and each drug was well tolerated.

Drug Information

43E. Accuracy of original research abstracts in pharmacy journals. *Leah G. Ward, Pharm.D.,* Michael G. Kendrach, Pharm.D., Sherry O. Price, R.N., Pharm.D.; Samford University; Birmingham, AL.

Presented at the Midyear Clinical Meeting of the American Society of Health-System Pharmacists, Atlanta, GA, December 2002.

44. Is the information there? Evaluation of personal digital assistant drug information software programs for anticoagulant and antithrombotic therapies. *Shelly J. Enders, Pharm.D.,* Jason M. Enders, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: This evaluation documents the breadth, clinical dependability, and information balance of palm operating system (Palm OS) personal digital assistant (PDA) drug-information software programs specific to anticoagulant and antithrombotic therapies.
METHODS: One hundred forty-one questions regarding anticoagulant and antithrombotic agents used for venous thromboembolic disorders and/or acute coronary syndromes were developed. Questions were derived from eleven pre-specified categories (e.g. dosing, administration, monitoring, etc.). Eleven PDA software programs were evaluated for information breadth (percentage of questions answered) and clinical dependability (percentage of questions factually complete) based on answers to the questions. Program answers were deemed factual when confirmed by two standard references. The balance of information was determined by calculating the average of information breadth and clinical dependability.
RESULTS: Breadth of information ranged from 42.5% to 83%; LexiComp Platinum was the most expansive program. Clinical dependability ranged from 80.7% to 98.1%; A to Z Drug Facts was the most clinically dependable program. However, A to Z Drug Facts provided the narrowest breadth of information. Mosby Drugs provided the least clinically dependable information. Lexi-Comp Platinum was again the leader in balance of information (88.1%) while Physician's Drug Handbook provided the least balanced information (67.8%).
CONCLUSIONS: The greatest breadth and balance of information regarding anticoagulant and antithrombotic therapies was provided by Lexi-Comp Platinum. A to Z Drug Facts contained the most clinically dependable information, yet provided the most narrow breadth. Overall, health care

professionals may find the greatest breadth and balance of anticoagulant and antithrombotic drug information when using Lexi-Comp Platinum.

45E. Direct-to-consumer advertising influence in family medicine residency training sites. *Rebecca L. Wood, Pharm.D.,* Sara L. Noble, Pharm.D., J. Anthony Cloy, M.D., Kentrell Liddell, M.D.; VA Jackson Medical Center; Ortho-McNeil Pharmaceuticals, Inc.; University of Mississippi Medical Center, Jackson, MS.

Presented at the 24th Annual Conference on Patient Education of the Society of Teachers of Family Medicine, Fort Lauderdale, FL, November 22, 2003.

46. A survey of response methods and response times for drug information departments in the pharmaceutical industry. *Jennica Lewis, Pharm.D.,* Carla Barrett, Pharm.D., Jacqui Collins, Pharm.D., Jenny Holabaugh, Arlene Santhouse, Pharm.D., Marcy Yanchunas, Pharm.D.; Wyeth Pharmaceuticals, St. David's, PA.

PURPOSE: To evaluate methods of response and response times of industry-based drug information departments to questions received from health care providers.
METHODS: A survey regarding the preparation, approval, and distribution of standard response letters (SRLs) was sent electronically using Zoomerang(TM) to drug information departments in pharmaceutical companies. The survey sample was selected to include companies of various sizes, as well as both pharmaceutical and biopharmaceutical companies.
RESULTS: Response rate to the survey was 71% (29/41 surveys). The most frequently used method of response to product inquiries is mail (79%), and most companies do not offer to fax information (76%). If information is faxed, about half (57%) also follow-up with a mailed response. All companies stated that a written response is sent within 5 days, with most forwarding the response in 2 days or less (86%). A total of 2 or 3 people must review a new SRL (52%), with an approval time of 1-2 weeks (41%). Requests for information received through the internet total 1 to 20 weekly for 62% of companies, with 14% of companies reporting more than 80 requests weekly. The most frequently used method of responding to inquiries from the internet is e-mail (46%), followed by phone (36%) and mail (21%). A majority of companies do not send SRLs through e-mail (69%). Most companies do not make SRLs accessible through the internet (86%).
CONCLUSIONS: Health care providers can expect to receive a response from an industry-based drug information department within 5 days. While the internet can be used to submit requests for information, responses are usually mailed.

Education

47. Evolution of clinical experiences for third-year students: increasing the application of clinical knowledge. Larry Aull, Pharm.D., MEd, *John T. Johnson, Pharm.D.,* Keith Herist, Pharm.D., Chris Cook, Ph.D., Pharm.D., Matt Perri, Ph.D., R.Ph., Jennifer L. Phillips, Pharm.D., Lori Duke, Pharm.D.; University of Georgia, Athens, GA.

PURPOSE: To evaluate student and preceptor perceptions of third year pharmacy students' clinical and communication skills and confidence after incorporating patient encounters into the lab experience. This curriculum change was made to prepare students for clerkship rotations and to apply classroom learning to real life situations.
METHODS: A change from a case study format to patient settings where students shadowed physicians, interviewed patients, wrote drug therapy recommendations to physicians, administered immunizations and performed health screenings was made for the third year lab. Student course evaluations have been assessed before and after these changes were made to see if the students perceive this as a positive change. A survey of preceptors will be conducted to assess their perception of improved skills by our students, since these changes have been made.
RESULTS: Analyzing student evaluations indicates that changing from a case study, problem based learning format to actual patient encounters and counseling has improved the students confidence level in communication with patients and health care providers and in the ability to transfer their clinical knowledge to these patients. From informal conversations, preceptors have told us that the students are better prepared for rotations due to these experiences. Data from the more formal evaluation is pending.
CONCLUSIONS: Incorporating actual patients care experiences into the third year lab has improved students' confidence and clinical skills, and has better prepared them for their clerkship experiences.

48E. Assessment of community pharmacists knowledge, skill, comfort and interest in performing cancer awareness and prevention activities. *William J. Spruill, Pharm.D.,* William E. Wade, Pharm.D.; University of Georgia, Athens, GA.

Published in Pharmacotherapy 2003;23(3):395-6.

49E. Board of Pharmaceutical Specialty certification and effects on academic units: a survey of deans of colleges and schools of pharmacy. Frank Romanelli, Pharm.D., Jeff J. Cain, B.S., Kelly M. Smith, Pharm.D., *Melody Ryan, Pharm.D.*; University of Kentucky, Lexington, KY.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, Minneapolis, MN, July 22, 2003.

50. Assessing the impact of osteoporosis education on knowledge retention and behavioral modifications in young adults. *Ashley D. Butler, Pharm.D.,* Keri Mattes, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: This study assessed young adults' pre-knowledge and understanding of osteoporosis and evaluated osteoporosis screening/educational methods to enhance knowledge retention and encourage positive behavioral change.
METHODS: 146 2nd-year college students voluntarily completed a pre-test assessing osteoporosis knowledge and a baseline behavior survey, related to reversible osteoporosis risk factors. Following pre-test/survey, all participants watched a 10-minute osteoporosis educational video. Of the 101 female participants, 46 were randomized to receive peripheral ultrasound bone mineral density (BMD) testing. Male participants did not receive BMD testing. After 10 weeks, all participants completed a post-test/survey to assess content retention and behavioral changes.
RESULTS: Two of three groups, BMD tested females and males, had a statistically significant increase in median test scores from pre to post-test ($p=0.008$ and $p=0.048$ respectively). Baseline behaviors were similar between all groups in relation to meeting pre-calcium/vitamin D requirements. 63% of participants did not meet RDA of calcium intake. No significant differences were observed between all groups for post-calcium/vitamin D intake ($p=0.072$ and $p=0.248$ respectively). Post surveys revealed no significant difference among individual groups for behavioral changes in tobacco and exercise habits. A significant relationship in change of alcohol ($p=0.007$) and caffeine ($p=0.02$) intake between groups was observed. However, the increase consumption among the male group likely accounted for this difference.
CONCLUSIONS: Increasing levels of knowledge about osteoporosis may not always be associated with influencing behaviors in young adults. However, because of the importance of building/maintaining an adequate bone mass in earlier years, educational interventions targeting our younger population are warranted.

51. Improving the understanding of geriatric needs in today's health care system through role-play: the Geriatric Medication Game®. Stephanie L. Evans, Pharm.D., *Myra T. Belgeri, Pharm.D.,* Patrick E. Fontane, Ph.D.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: To increase pharmacy students' understanding of geriatric needs in today's health care system through role-play.
METHODS: Forty-two students from the first professional year at the St. Louis College of Pharmacy participated in the Geriatric Medication Game®. The game uses role-playing to improve players' understanding of obstacles confronting older persons, including the use of medications. Players were provided with everyday situations that elderly persons encounter in our health care system. All players completed pre and post questionnaires that assessed their attitudes and experiences. The players were asked to use a Likert-type scale (ranging from 1 to 5) to rate the level of emotions they experienced and their awareness of geriatric needs.
RESULTS: More than 75% of students reported the game helped them to empathize with elderly patients and improved their understanding of how to help elderly patients in our health care/pharmacy system. Sixty percent experienced high levels of frustration (4 or 5), and only 10% reported no frustration. Forty-eight percent reported no sadness (mean 1.9). These emotions were consistent with the design of the experience. Students recognized that elderly persons have difficulty utilizing the health care system, including financial, transportation, and medication obstacles. All students reported at least some increase in awareness of problems encountered by elderly persons (mean 4.1).
CONCLUSIONS: The Geriatric Medication Game provides an opportunity for pharmacy students and other health care providers to role-play an older person in the health care system. This increases awareness of perceptions and experiences of older persons and can be a resource for improving the care of older patients.

52. Nuclear pharmacy education in ACPE-accredited colleges of pharmacy. *Edward M. Bednarczyk, Pharm.D.,* Dmitri Mayer, B.S., Lai Kuen Wong, Pharm.D. candidate; University at Buffalo, State University of New York, Buffalo, NY.

PURPOSE: Ten to twelve million nuclear medicine procedures are performed annually in the U.S., each of which requires administration of a radiopharmaceutical. While the entry level doctor of pharmacy degree was intended to raise the level of practice throughout the profession, some areas of specialty practice may be perceived as expendable, and de-emphasized or eliminated from the curriculum. This study was undertaken to determine the current status of instruction in nuclear pharmacy practice in schools of pharmacy.
METHODS: A survey was sent to the academic deans of the 91 ACPE-

accredited schools in the U.S. and Canada. The survey consisted of ten questions about the teaching of nuclear pharmacy practice. Schools were asked if instruction was offered, and where in the curriculum instruction was included.
RESULTS: Seventy five (82.4%) schools responded. Of these, 45 (60%) offer no instruction in nuclear pharmacy in any portion of the curriculum. Among the 30 (40%) offering instruction, the majority of instruction was focused on the dispensing of radiopharmaceuticals and/or radiation safety. Only 10 programs reported teaching nuclear pharmacy material relevant to generalists (i.e., pharmacokinetic distribution or drug interactions). The current level of instruction represents a sharp decline from 1981 when nearly 90% of schools reported inclusion in the curriculum.
CONCLUSIONS: The majority of graduates from ACPE-accredited schools of pharmacy are not presented with any instruction in radiopharmaceuticals in spite of the number of patients receiving these drugs. Lack of knowledge of these agents is likely to have an adverse impact on pharmaceutical care.

53. Effect of topiramate on nitroglycerin induced headache in migraineurs; assessment by $H_2{}^{15}O$ positron emission tomography. *Edward M. Bednarczyk, Pharm.D.,* Linda Hershey, M.D., Ph.D., David Wack, M.S., Jayakumari Gone, M.D.; University at Buffalo, Buffalo, NY.

PURPOSE: Nitroglycerin (GTN) is widely used as an experimental model of acute migraine headache. Little is known about this model in migraineurs or with drug therapy. We studied the influence of topiramate (TOP) on global and regional cerebral blood flow (CBF, rCBF) in migraineurs using the GTN model.
METHODS: Migraineurs (migraine with or without aura, IHS criteria) were studied. Subjects with significant neurologic, psychiatric, or other medical conditions were excluded. Other than topiramate, no prophylactic or analgesic medications were permitted at the time of study. CBF and rCBF were measured at baseline, following IV GTN at 0.125, 0.25, and 0.5 µg/kg/min, and 30 and 60 minutes following termination of GTN. rCBF was determined by statistical parametric mapping. Scanning was repeated 8 weeks after titration of topiramate up to 200 mg/day.
RESULTS: Nine subjects were studied on and off topiramate. Subjective pain scores were lower on topiramate. Mean CBF (ml/min/100g (SD)) were as follows.

	Baseline	GTN 0.125*	GTN 0.25	GTN 0.5	30min p GTN*	60 min p GTN
Pre TOP	48 (6)	51 (6)*	53 (8)	51 (1)	54 (8)*	51 (11)
Post TOP	49 (9)	60 (12)	54 (8)	53 (9)	57 (9)	50 (6)

*p<0.05 compared to baseline

GTN increased rCBF in areas included the pons (p=0.022) and the anterior ciguatera gyri (p=0.004) prior to and following topiramate. Significant reductions in rCBF were identified in the left temporal and occipital lobes following GTN, however these were absent following topiramate.
CONCLUSIONS: In migraineurs, topiramate decreases severity of GTN induced HA and appears to moderate reductions in rCBF.

54. Taking call as pharmacy students: a survey of pharmacists' opinions of the experience. *Kimi S. Vesta, Pharm.D., BCPS,* Kevin C. Farmer, Ph.D., Wanda J. Kilzer, Pharm.D., BCPS; University of Oklahoma, Oklahoma City, OK.

OBJECTIVE: Survey perceived benefits and limitations of pharmacy students taking call with the medicine team while in the Doctor of Pharmacy (Pharm.D.) program.
METHODS: Questionnaires were mailed to alumni who completed an Adult Medicine rotation offering an on-call experience. Responses for each item were summated and means determined for entry-level, track-in, and post-baccalaureate Pharm.D. students. Kruskal-Wallis compared median responses between groups.
RESULTS: Sixty-nine surveys were mailed, and 55% responded. Of the post-baccalaureate alumni, 78% responded, 93% took overnight call, and 79% were on-call ≥ four nights. All track-in alumni took overnight call, and 85% were on-call ≥ three nights. Ninety percent of entry-level alumni took evening call, and 90% were on-call ≤ two nights. Responses did not vary significantly between groups; although sample size limits the power to detect small differences. Alumni agreed they learned more about diseases, health care logistics, and the impact of hospitalization on the patient because of taking call. It was not felt to negatively impact their rotation performance, financial or family obligations, or safety. All agreed taking call was a team-building experience and would encourage students to take call. Comments from alumni with negative opinions suggest defining expectations of the pharmacy student's role while on-call to the student and team would improve the experience.
CONCLUSIONS: Trends between programs in on-call types and numbers suggest they are not providing similar educational experiences. Taking call provides the pharmacy student with a unique experience to learn about diseases, acute care, and building professional relationships within the health care team.

55. An evaluation of objective structured clinical evaluations as part of an ambulatory care rotation. *Joli D. Fermo, Pharm.D., BCPS, CDE, BC-ADM,* Stacy M. Prutting, Pharm.D., BCPS, CDE, Kelly R. Ragucci, Pharm.D., BCPS, CDE, Jennifer N. Mazur, Pharm.D., CDE; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate student and resident learners' perceptions of objective structured clinical examinations (OSCEs) upon completion of an ambulatory care rotation.
METHODS: OSCEs are conducted at the end of each ambulatory care rotation to directly observe and evaluate learner performance in standardized, mock, clinical pharmacy scenarios. Learners were requested to evaluate OSCEs via an on-line anonymous evaluation using a 5-point Likert scale and open-ended questions. Specifically, learners were asked questions regarding preparation of OSCEs, confidence in dealing with the clinical situations, enhancement of their ambulatory care skills, representation of actual clinical scenarios, feedback received, and overall perceptions. Results were compiled and analyzed over a 12-month time frame and are reported using descriptive statistics.
RESULTS: Forty-three evaluations (93%) were collected over a one-year period. Eighty-six percent of learners agreed or strongly agreed that OSCEs increased their level of confidence in dealing with clinical situations and 83% percent stated that OSCEs enhanced their ambulatory care skills. Ninety-five percent of learners agreed or strongly agreed that OSCEs represent actual clinical situations. Ninety-eight percent thought that the feedback they received was adequate. Most learners stated that they prepared for OSCEs by studying a CD-ROM, created by ambulatory care preceptors, and/or through patient encounters in clinic. Overall, learners believed that the scenarios represented actual clinical situations and appreciated the immediate feedback. Suggestions for improvement were station-specific and without commonality.
CONCLUSIONS: Student and resident learners' perceptions of OSCEs were positive and affirm continuation of this learning experience. Station-specific recommendations will be shared with all ambulatory care preceptors.

56E. Clerkship grades: do they inflate students' GPA? *Philip D. Hall, Pharm.D.,* George E. Francisco, Pharm.D.; Medical University of South Carolina, Charleston, SC; University of Georgia, Athens, GA.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, Minneapolis, MN, July 19-23, 2003.

57. Development of an experiential teaching assessment tool. Craig D. Cox, Pharm.D., *Brad L. Stanford, Pharm.D., BCOP,* Sara Brouse, Pharm.D., BCPS, Charles F. Seifert, Pharm.D., FCCP, BCPS, Krystal K. Haase, Pharm.D., BCPS, Ronda L. Akins, Pharm.D., Venita L. Bowie, Pharm.D., James P. Tsikouris, Pharm.D., Anthony J. Busti, Pharm.D., BCPS, Sachin Shah, Pharm.D., Ronald Hall, Pharm.D.; Texas Tech University, Amarillo, TX; Texas Tech University, Dallas, TX; Texas Tech University, Lubbock, TX.

PURPOSE: Documentation of excellence in teaching plays a pivotal role in the promotion process of pharmacy practice faculty. Many methods exist for assessment of didactic teaching, while evaluation of experiential teaching has proven more difficult. Therefore, we designed an evaluation form for peer review of clerkship teaching at our institution.
METHODS: The internal medicine team, consisting of pharmacy practice faculty members from three campuses, determined which teaching abilities they deemed most critical for a successful clerkship experience. This information, coupled with the characteristics of a quality preceptor identified from primary literature were used to develop the assessment tool.
RESULTS: A 4-page, peer review evaluation form was developed, consisting of 13 essay and 11 multiple choice questions. These questions allow fellow faculty members to collect demographic information and evaluate three areas of preceptor and student interaction: clinical duties, discussion/meeting activities, and overall assessment of important preceptor qualities. [Assessment tool will be provided with poster]
CONCLUSIONS: This form may be applicable to faculty with varying practice site/clerkship responsibilities and can serve as documentation of clerkship teaching ability. In addition, the form may provide increased consistency in pharmacy student education among a variety of practice sites.

58. Telepharmacy from classroom to practice: a pilot study. *Charles F. Seifert, Pharm.D.,* Michael A. Veronin, Ph.D., Roland A. Patry, M.S., Dr.P.H., Donald B. McBeath, Jon C. Phillips, Sidney C. Ontai, M.D., M.B.A., T. Diane Kretschmer, R.Ph., Patti J. Patterson, M.D., M.P.H.; Texas Tech University Health Sciences Center, Lubbock, TX; Texas Tech University Health Sciences Center, Amarillo, TX; Sidney Ontai MD Association; Plainview, TX.

BACKGROUND: West Texas comprises 50% of the land mass and 13.9% of the total population of the state. In this area, 80 counties are medically underserved: 54 suffer primary care shortages, 37 have no hospital, and 19 have no pharmacist. To date, no School of Pharmacy in the U.S. allows students to care for patients in a telepharmacy setting as part of a required Rural Clerkship.
PURPOSE: To implement a teaching model of telepharmacy with a practice component for 4th year Pharm.D. students, analyze public policies and formulate strategies for future research.
METHODS: A televideo-based system of remote dispensing that complies

with Texas pharmacy law was established with the Turkey Medical Clinic in Turkey, TX and the Texas Tech Medical Center Southwest Pharmaceutical Care AND Infusion Center in Lubbock. A 6-hour didactic session with "hands on" experience was provided for the 3rd year Doctor of Pharmacy students on the Lubbock Campus in June of 2002 prior to starting full-time 4th year clerkships. During their 4th year required Rural Clerkship the students on the Lubbock campus spent 1 week each with the pharmacy and rural health clinic providing telepharmacy services.
RESULTS: The first telepharmacy prescription in the State of Texas was dispensed at the Turkey Medical Clinic from Texas Tech on September 18, 2002. As of April 30, 2003, 295 telepharmacy prescriptions have been dispensed to the Turkey site. As of April 30, 2003, 14 students have spent time with telepharmacy as part of their Rural Clerkship. Student evaluations of the didactic course were excellent (2.82/3.0) and clerkship evaluations were fair to good (2.64-3.62/5.0).
CONCLUSIONS: Telepharmacy in concert with telemedicine in remote areas can function as a practical clerkship training site for Pharmacy students.

Emergency Medicine

59E. An evaluation of antibiotic use in the emergency department. *Ashley S. Trask, Pharm.D.,* Jeffrey King, Pharm.D., Robert W. Derlet, M.D., Hien Nguyen, M.D.; University of California Davis Medical Center, Sacramento, CA.

Presented at the Western States Conference, Asilomar, CA, May 21, 2003.

Endocrinology

60E. Insulin detemir pharmacokinetics, pharmacodynamics, safety, and tolerability profiles are similar in healthy Caucasian and Japanese-American subjects. *Stan S. Jhee, Pharm.D.,* William H. Lyness, Ph.D., Patrick B. Rojas, Ph.D., Mark T. Leibowitz, M.D., Victoria Zarotsky, Pharm.D., Lisbeth V. Jacobsen. M.S.C.; California Clinical Trials, Beverly Hills, CA; Novo Nordisk Pharmaceuticals, Inc., Princeton, NJ; Novo Nordisk Pharmaceuticals, A/S, Bagsvaerd, Denmark.

Published in Diabetes Journal, June 2003(supplement);1944.

61E. Vardenafil improved satisfaction with erectile hardness, orgasmic function, and sexual experience in men with diabetes with erectile dysfunction. Jay M. Young, M.D., Irwin Goldstein, M.D., Jerome S. Fischer, Thomas Segerson, Terry Taylor; South Orange County Medical Associates, Laguna Woods, CA; Boston University, Boston, MA; Diabetes and Glandular Disease Clinic, San Antonio, TX; Bayer Corporation, West Haven, CT.

Presented at the Annual Meeting of the American Diabetes Association, New Orleans, LA, June 13-17, 2003.

62. Incidence of congestive heart failure-related interventions in patients receiving rosiglitazone and insulin. *Jennifer R. Marceille, Pharm.D., BCPS,* Janelle Goins, Pharm.D., BCPS, Rita Soni, Pharm.D., BCPS, Joseph Biery, Pharm.D., GCP, Todd A. Lee, Pharm.D., Ph.D., Edward Hines, Jr. VA Hospital, Hines, IL.

PURPOSE: A retrospective pre/post cohort study to assess the relationship of the addition of rosiglitazone to diabetic patients receiving insulin and the development or worsening of congestive heart failure (CHF) symptoms.
METHODS: A list of patients receiving insulin therapy who were subsequently prescribed rosiglitazone prior to September 30, 2001 was generated from prescription files at Hines VA. The date rosiglitazone was prescribed was considered the index date. Medical records were reviewed for six months prior to and six months after the index date to assess 1) the number of patients with a diagnosis of CHF and 2) the number of documented patient complaints of CHF symptoms requiring a medical intervention (i.e., unscheduled primary care/ emergency room visit, initiation/ dose adjustment of CHF pharmacotherapy, or hospitalization).
RESULTS: A diagnosis of CHF was documented in 25% of patients in the pre-index period and 30% in the post-index period. Of 139 patients, 36% had a medical intervention for CHF symptoms in the post-index period vs only 14% in the pre-index period ($p<0.0001$). Of the 50 patients requiring a medical intervention in the post-index period, 33 did not have an intervention in the pre-index period.
CONCLUSIONS: This study shows an association to develop signs or symptoms of CHF in patients receiving insulin therapy after rosiglitazone is prescribed. These results may support the FDA warning of an increased risk of cardiac failure in patients receiving both rosiglitazone and insulin, as noted in the Avandia® (rosiglitazone) product information.

63. The efficacy of insulin glargine in the treatment of diabetes. Jeffrey S. Stroup, Pharm.D., *Michael P. Kane, Pharm.D., BCPS,* Robert S. Busch, M.D., Gary Bakst, M.D., Robert A. Hamilton, Pharm.D.; Albany College of Pharmacy, Albany, NY.

PURPOSE: A decreased incidence of hypoglycemia with insulin glargine compared to NPH insulin has been well documented, but a difference in efficacy has not. The purpose of this study was to compare the one-year efficacy of insulin glargine to NPH insulin in diabetes patients in a private endocrinology practice.
METHODS: A retrospective review was undertaken of 244 patients with a minimum one-year duration of diabetes, who were first prescribed insulin glargine in 2001-2002. Patients included those with Type 1 diabetes (on insulin therapy) or Type 2 diabetes (on oral medications only, on combination oral/insulin therapy, or receiving insulin only) treated with insulin glargine for one year. The primary endpoint was HbA_{1C}.
RESULTS: 197 of the identified 244 patients were evaluable for comparison. Overall, HbA_{1C} significantly decreased by 0.53 ± 1.4% ($p<0.001$) from a baseline mean of 8.1± 1.7%. In Type 2 patients previously treated with NPH insulin (n=129), HbA_{1C} decreased by a significant 0.57 ± 1.5% ($p<0.001$). HbA_{1C} decreased 0.71 ± 1.3%, ($p=0.0043$) in Type 2 patients previously receiving oral agents only (n=33). Type 1 patients demonstrated no significant change in HbA_{1C} (-0.22 ± 1.0%, $p=0.217$, n=35). Overall, there was no significant change in daily insulin dosage during the 1-year period, nor were there any significant changes in weight in any of the groups over this time.
CONCLUSIONS: The use of insulin glargine in Type 2 diabetes patients was associated with a significant reduction in HbA_{1C}.

64. Two-year follow up of aspirin use among an ambulatory population of patients with diabetes. John J. Faragon, Pharm.D., *Nancy M. Waite, Pharm.D.,* Eric H. Hobson, Ph.D., Hope Murphy, Pharm.D., Hedy Migden, M.D.; Albany College of Pharmacy, Albany, NY; Altamont Internal Medicine and Pediatrics, Altamont, NY.

PURPOSE: A previous pharmacist-initiated telephone and clinic intervention in patients with diabetes resulted in improved aspirin use from 33% to 82% of eligible patients. A follow-up assessment was conducted two years post intervention.
METHODS: Patients involved in the initial intervention were re-contacted by a pharmacist using a structured telephone interview to determine their current aspirin use.
RESULTS: Of 27 patients who accepted the recommendation to begin aspirin therapy during routine clinic visits, 18 were still taking daily aspirin, 4 were lost to follow-up, 3 were not taking aspirin, 1 patient was hospitalized, and 1 patient was deceased. Of 15 patients who accepted the recommendation via telephone, 6 patients were still taking daily aspirin, 4 were lost to follow-up, 3 were deceased, and 2 patients were not taking aspirin. Difference in the rates of aspirin use in both intervention groups was not significant ($p=0.178$). Of the 28 patients who reported that they were already taking daily aspirin therapy prior to the intervention, 16 were still taking aspirin, 10 were lost to follow-up, 1 refused to comment, and 1 had stopped aspirin due to concurrent warfarin therapy. Excluding patients lost to follow up or deceased, 40/48 (83%) of patients remain on aspirin.
CONCLUSIONS: A two-year follow-up interview conducted via telephone demonstrated that over time pharmacist-initiated interventions to improve rates of aspirin use in the clinic or via telephone remained effective.

65. Caring for poorly-controlled diabetes: a randomized, controlled pharmacist intervention. *Peggy Soule Odegard, Pharm.D., BCPS, CDE,* Shelly Gray, Pharm.D., MS, BCPS, Alvin Goo, Pharm.D., CDE, Jeff Hummel, M.D.; University of Washington; Harborview Medical Center, Seattle, WA.

PURPOSE: The primary objective was to improve diabetes control in adults with poorly-controlled type 2 diabetes mellitus (hemoglobin A_{1c} [A_{1c}] ≥ 9.0%) using a pharmacist intervention. The secondary objective was to evaluate whether medication appropriateness was improved.
METHODS: This study was a randomized, multi-clinic, controlled trial in 75 subjects recruited from University of Washington Physician Network primary care clinics. The 6-month intervention involved: 1) collaboration with the provider to optimize therapy, and 2) weekly to monthly contact with subjects to promote medication adherence and safety. Medication and patient related variables were collected during the baseline interview. A_{1c} and medication appropriateness were determined at baseline and 6 months. Difference in A_{1c} between intervention and control groups was assessed controlling for baseline value and clinic.
RESULTS: The intervention and control groups were similar at baseline in mean age (52 years), A_{1c} (10.5 vs 10.1), mean number of scheduled medications (6.1 vs 5.9), and proportion having ≥ 1 inappropriate medication (48% vs 52%). There was no statistically significant difference in A_{1c} in the intervention versus control group at 6 months as compared to baseline. There was a greater improvement in medication appropriateness in the intervention versus control (mean change score -0.26 vs -0.05, respectively) although this was not statistically significant ($p>0.05$).
CONCLUSIONS: The pharmacist intervention did not improve diabetes control for subjects during the intervention phase. Methods to improve control of poorly controlled diabetes need further study.

66E. Impact of different insulin glargine regimens on glycemic parameters in intensively treated adults with type 1 diabetes. Anna D'Souza, M.S.,

Kenneth E. Izuora, M.D., Mary E. Hisatomi, B.A., Halsley Hoff, B.A., Peter A. Gottlieb, M.D., Laura Antell, M.B.A., M.P.H., H. Peter Chase, M.D.; West Virginia University, Morgantown, WV; Barbara Davis Center for Childhood Diabetes, Denver, CO; University of Colorado Health Sciences Center, Denver, CO; Aventis Pharmaceuticals, Bridgewater, NJ.

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Gastroenterology

67. Faster in vitro biotransformation of s-omeprazole by the cytochrome P450 isoenzyme system compared to pantoprazole. *Dr. Wolfgang Alexander Simon*; ALTANA Pharma AG, Konstanz, Germany.

PURPOSE: Proton pump inhibitors (PPIs) are metabolized by cytochrome P450 (CYP) isoenzymes CYP 2C19 and CYP 3A4. It was claimed that S-OME is predominantly metabolized by CYP 2C19, with CYP 3A4 playing only a minor role.
METHODS: Comparison of the metabolism of s-omeprazole (S-OME), r-omeprazole (R-OME) and pantoprazole (PANTO) in (I) human liver microsomes, (II) human recombinant CYP 2C19 isoenzyme and (III) human recombinant CYP 3A4 isoenzyme. Incubation: S-OME, R-OME and PANTO (10mM each) in presence of 1.0 mg (I), 0.1(II) and 0.3 (III) mg protein/ml, 100 mM Tris-HCl, pH 7.4, 1 mM NADPH2). Reaction was terminated by liquid nitrogen, parent compound was detected by HPLC (10 mM KH2PO4, pH 7.4, acetonitrile gradient 20-48%).
RESULTS: I) In human liver microsomes, degree of metabolism increased from PANTO over S-OME to R-OME, resulting in reduction of the parent compound of 44%, 62% and 66%, respectively, after 120 min. II) In recombinant CYP 2C19, PANTO and S-OME were similarly at all time-points, whereas R-OME reached a high level of metabolism after only 30 minutes. III) In recombinant CYP 3A4, PANTO showed a lower metabolic rate than S-OME after 30 and 120 minutes (13% and 22% for PANTO, 53% and 80% for S-OME, respectively). R-OME was metabolized similarly to S-OME.
CONCLUSIONS: In human liver microsomes, S-OME and R-OME were metabolized to a higher extent than PANTO. In recombinant CYP 2C19, S-OME and PANTO showed similar metabolic rates, while R-OME was metabolized faster than PANTO. Also, in recombinant CYP 3A4, S-OME and R-OME were metabolized faster than PANTO. Overall, these in vitro results show faster cytochrome P450 biotransformation rate for S-OME and R-OME compared to PANTO. Clinically, this may lead to a higher drug interaction risk for S-OME.

68E. A novel option in proton pump inhibitor dosing: lansoprazole orally disintegrating tablet (Prevacid® SoluTab™) dispersed in water and administered via oral syringe. David A. Gremse, M.D., Brendan J. Colgan, M.B., MRCGP, Joan R. Donnelly, BSMT, *Curt R. Griffith, Pharm.D.,* Michael J. Kukulka, B.S., Chang Q. Lee, M.D., Ph.D., Eric Lloyd, M.S.; University of Southern Alabama, Mobile, AL; MDS Pharma Services, Belfast, United Kingdom; TAP Pharmaceutical Products Inc., Lake Forest, IL.

Presented at the 15th Annual Meeting of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, San Antonio, TX, October 24-27, 2002.

69E. Intravenous and oral lansoprazole are equivalent in suppressing stimulated acid output in patients with erosive esophagitis. Thomas O.G. Kovacs, M.D., *Calvin Y. Chao, M.D.,* Yi-Lin Chiu, Ph.D., Betsy L. Pilmer, R.N., B.S.N., David C. Metz, M.D.; VA Greater Los Angeles Healthcare System, Los Angeles, CA; TAP Pharmaceutical Products Inc., Lake Forest, IL; Abbott Laboratories, Abbott Park, IL; University of Pennsylvania, Philadelphia, PA.

Presented at the Annual Meeting of Digestive Disease Week, Orlando, FL, May 17-22, 2003.

70. Long-term outcomes of patients treated for *Helicobacter pylori* infection at a veterans affairs medical center. *Marisel Segarra-Newnham, Pharm.D., M.P.H., BCPS,* Elizabeth Johanson, Pharm.D.; Veterans Affairs Medical Center, West Palm Beach, FL.

PURPOSE: Describe the long-term outcomes of patients treated in a pharmacist-managed *Helicobacter pylori* (HP) clinic.
BACKGROUND: An HP clinic was created in 1996 at a VA. Patients receive clarithromycin/amoxicillin-based therapy according to the clinic protocol. Clarithromycin use is restricted to treatment of HP infection. Metronidazole is used instead of amoxicillin in penicillin allergic patients. Results at one year showed that 53% of the patients were able to stop chronic heartburn therapy. Outcomes beyond one year are not known.
METHODS: The electronic records of patients treated at the HP clinic from June 1996 to March 2001 were evaluated. Patients with at least 2 years of follow-up information were included. Baseline demographic and long-term outcome data were collected. Discontinuation rate, failure rate and need for re-treatment were evaluated.
RESULTS: Out of 229 patients treated during the period studied, 198 had at least 2 years of information. Of these, 177 were men and 21 were women. Three of the 198 patients (1.5%) were unable to complete antibiotic therapy with one needing a hospital admission for severe reflux symptoms four years after treatment. Re-infection with HP was not documented. The other three patients are stable on chronic acid suppressive therapy. Five patients, two of them women, failed an initial course to eradicate HP (2.5%). After treatment with bismuth-based therapy, four of the five had documented eradication of infection. Forty-four percent of patients were off chronic therapy at time of last review.
CONCLUSIONS: A pharmacist-managed HP treatment clinic can facilitate discontinuation of chronic acid suppressive therapy in over a third of patients. A low treatment failure rate was found in our population. The rate is below the national average of 10-20% for clarithromycin-based regimens, possibly due to restriction of clarithromycin at our facility.

71E. Lansoprazole provides gastroprotection in high-risk arthritis patients taking daily aspirin and chronic NSAIDs. Jay L. Goldstein, M.D., Nancy Joseph-Ridge, M.D., Patricia A. MacDonald, R.N., B.S.N., Bidan Huang, Ph.D. Cynthia M. Collis, *Calvin Y. Chao, M.D.,* E. David Ballard, II, M.D.; University of Illinois, Chicago, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL; Abbott Laboratories, Abbott Park, IL.

Presented at the Annual Meeting of the American College of Rheumatology, Orlando, FL, October 23-28, 2003.

72. Preparation and evaluation of an extemporaneous suspension sontaining lansoprazole orally disintegrating tablets (Prevacid® SoluTab™): an in vitro study. *Rajneesh Taneja, R.Ph., Ph.D.,* Joseph A. Scarim, B.S.; TAP Pharmaceutical Products Inc., Lake Forest, IL; JSAS Services, Mundelein, IL.

PURPOSE: Determine the feasibility of preparing an extemporaneous suspension containing lansoprazole orally disintegrating tablet (LODT), water and OraPlus and the suitability for dispensing doses <15 mg. LODT contains enterically coated lansoprazole microgranules.
METHODS: LODT 15 mg and 1 ml of water were transferred into a 25-ml dispensing bottle, swirled for 1 minute, 14 ml OraPlus added, and the bottle shaken for 1 minute. Acid resistance test (0.1 N HCl for 1 hour, n = 5) was performed on the suspension versus intact LODT (reference) to determine the integrity of the microspheres. Lansoprazole was quantified by liquid chromatography and compared with theoretical content. The suspension was prepared for each aliquot, held for 10 minutes and shaken immediately before withdrawal.
RESULTS: Suspending LODT in water and OraPlus for 10 minutes had no significant impact on microgranule integrity. Lansoprazole content after the acid resistance test for the suspension and reference was comparable (90.7 (± 2.6) and 91.3 (± 1.9), respectively). Table 1 summarizes dose uniformity results.

		Lansoprazole Content		
		Theoretical	Experimental	% Expected
Aliquot Volume (ml)	n	(mg)	(SD*) (mg)	Dose
5	5	5.0	5.0 (0.3)	96.7
7.5	5	7.5	7.9 (0.2)	105.6
10	5	10.0	10.3 (0.4)	102.5

*standard deviation

CONCLUSIONS: This suspension containing lansoprazole orally disintegrating tablet, water and OraPlus is stable for at least 10 minutes. Aliquots can be withdrawn for dispensing fractions of the 15 mg lansoprazole dose, which may be beneficial for administering divided doses. Funded by TAP.

73. Feasibility of dosing lansoprazole orally disintegrating tablets (Prevacid® SoluTab™) via nasogastric tube: an in vitro study. *Rajneesh Taneja, R.Ph., Ph.D.,* Dean I. Shaffer, Ph.D., Joseph A. Scarim, B.S.; TAP Pharmaceutical Products Inc., Lake Forest, IL; JSAS Services, Mundelein, IL.

PURPOSE: Administering solid oral dosage forms can be challenging in patients with nasogastric (NG) tubes or swallowing difficulties. This study explored the feasibility of dispersing lansoprazole orally disintegrating tablet (LODT) in water and administering it through an NG tube. LODT contains enterically coated lansoprazole microgranules.
METHODS: LODT 30 mg tablet and 10 ml water were gently swirled for 1 minute in a 20-ml syringe barrel, and the resulting dispersion was injected through NG tubes (8F, 107 cm) followed by a 5 ml flush of water. The integrity of the enteric coat on the suspended microgranules delivered through the NG tube (test) versus the intact LODT (reference) was evaluated by an acid resistance test conducted in 0.1 N HCl for 1 hour. The quantification of lansoprazole was performed by liquid chromatography.
RESULTS: Suspending LODT in water and administering through an 8F NG tube had no significant impact on the integrity or the drug release characteristics of the lansoprazole microgranules (Table). Drug recovery from both the syringe and the NG tube was virtually complete.

Statistical Descriptor	Reference	Test Sample
n	6	6
mean	93.2	92.2

Standard deviation	1.9	2.1

CONCLUSIONS: Results indicate that lansoprazole orally disintegrating tablet can be dispersed in water and administered through an 8F NG tube or via syringe. This method may offer a dosing alternative for patients with a nasogastric tube or swallowing difficulties. Funded by TAP.

74E. Alternative methods of lansoprazole administration. Sandeep K. Gupta, M.D., Yi-Lin Chiu, Ph.D., Roberta G. Keith, R.N., B.S.N., *Anil Vootkur, Pharm.D.,* Joseph F. Fitzgerald, M.D.; Riley Children's Hospital, Indianapolis, IN; Indiana University, Indianapolis, IN; Abbott Laboratories, Abbott Park, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL.

Presented at the 15th Annual Meeting of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, San Antonio, TX, October 24-27, 2002.

75. Two-minute infusion of pantoprazole is as well-tolerated as the 15-minute infusion. Polly D. Fraga, M.D., Marlynne Micalizzi, R.N., B.S.N., *Xu Meng, Ph.D.*; Wyeth Research, Collegeville, PA.

IV pantoprazole (IVP) administered as a 15-minute infusion is approved for control of gastric acid secretion in GERD and ZES patients unable to take oral medication. This study compares the safety and tolerability of 80mgIVP administered as a 2-minute vs 15-minute infusion.
In a single-blind, randomized, multiple-dose, parallel-group study, 48 healthy subjects (aged 18-45) were randomly assigned for treatment with 80mgIVP infused for 2 or 15 minutes QD for 7 days. A blinded evaluator assessed the injection site for phlebitis and infiltration on a 5-point scale at specified intervals. Subjects completed the Visual Analogue Scale (VAS) for pain and burning at baseline and 5 minutes postinjection.
Over 99% of the infiltration scores and >95% of the phlebitis scores were rated zero. Forty-one scores of 1 and 1 score of 2 were from 12 subjects in the 2-minute group, and 20 scores of 1 and 10 scores of 2 were from 8 subjects in the 15-minute group. VAS assessment showed that the perception of pain and burning was no greater in the 2-minute group. The difference in AEs was not significant; all were mild or moderate except for 1 subject in the 15-minute group with elevated CPK, ALT, and AST that resolved spontaneously. Headache was the only event occurring in more than 1 subject.
The safety and tolerability of IVP as a 2-minute infusion is similar to the 15-minute infusion. A 2-minute infusion could aid hospital staff, eliminating the need for an infusion pump and additional admixture of the suspended drug.

76E. Rationale for changing proton pump inhibitor therapy: an intraindividual analysis of gastric acid suppression following treatment with different proton pump inhibitors. Philip O. Katz, M.D., *Albert Roach, Pharm.D.,* Philip B. Miner, Jr., M.D., Clive H. Wilder-Smith, M.D., Yusong Chen, Ph.D., Mark B. Sostek, M.D.; Graduate Hospital, Philadelphia, PA; AstraZeneca L.P., Wilmington, DE; Oklahoma Foundation for Digestive Research, Oklahoma City, OK; Berne University, Berne, Switzerland.

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77. An evidence-based approach provides a quantitative assessment of the efficacy of esomeprazole for healing of erosive esophagitis based on disease severity. David A. Johnson, M.D., *Albert Roach, Pharm.D.,* Barry M. Traxler, B.S., Douglas Levine, M.D.; Eastern Virginia School of Medicine, Norfolk, VA; AstraZeneca L.P., Wilmington, DE.

PURPOSE: Number needed to treat (NNT) provides an estimate of the number of patients who need to be treated with a drug to avoid an adverse outcome on alternate therapy. This quantitative analysis focused on treatment responses to proton pump inhibitors according to disease severity.
METHODS: Efficacy data from four clinical trials using once-daily esomeprazole 40 mg compared with omeprazole 20 mg (n=3) and lansoprazole 30 mg (n=1) for treatment of erosive esophagitis (EE) were identified. EE was graded A–D using the Los Angeles (LA) classification. For each trial we calculated the therapeutic gain, the absolute risk reduction (ARR) and the number needed to treat (NNT) for healing EE at week 8, for all patients (LA Grades A-D) and separately for those with severe disease (LA Grades C and D).
RESULTS: For all grades of esophagitis, the therapeutic gain achieved with esomeprazole was 9.5%, 7.2% and 2.4% versus omeprazole, and 3.8% versus lansoprazole. The NNT with esomeprazole for severe disease ranged between 5 and 10 relative to omeprazole. The NNT with esomeprazole for severe disease was 8 relative to lansoprazole, indicating that for every 8 patients treated with esomeprazole, 1 treatment failure with lansoprazole may be prevented.
CONCLUSIONS: Treatment with esomeprazole provided therapeutic gain regardless of the baseline severity of EE compared with lansoprazole and omeprazole. Because the severity of clinical symptoms is not predictive of disease severity, treatment with the most effective agent appears to be a rational therapeutic decision as supported in this evidence-based approach.

Geriatrics

78E. Medication health safety: assessing patient risk of drug-related problems by level of medical care. *Steven L. Clause, Pharm.D.,* Darren M. Triller, Pharm.D., Colleen P.H. Bornhorst, R.N.; Albany College of Pharamacy, Albany, NY; Northeast Health, Troy, NY.

Presented at the 19th International Conference on Pharmacoepidemiology and the 1st International Conference on Risk Management, Philadelphia, PA, August 2003.

79. An evaluation of frail elderly hypertensive patients in a PACE program: phase 2. *Karen H. McGee, Pharm.D.,* Janet M. Thames, Pharm.D., Heather R. Ashton, Pharm.D., Timothy A. Mullenix, Pharm.D.; University of South Carolina; Palmetto SeniorCare; Pfizer, Ind., Columbia, SC.

PURPOSE: The PACE (Program for All Inclusive Care of the Elderly) Program is a nationally recognized model for providing all inclusive medical care to the elderly while their caregivers work. A previous evaluation was completed to assess hypertension management in this frail elderly population. After aggressive interventions by pharmacists, a follow-up evaluation was completed.
METHODS: Recommendations for change in blood pressure medications were made by pharmacists from Phase 1 data. Phase 2 blood pressure measurements were collected over a six-month period. Patient's current antihypertensive medication regimens were recorded and blood pressure measurements were taken. Goal BP was defined as equal to or less than 140/90.
RESULTS: A total of 185 out of 220 frail elders were available for follow-up from the Phase 1 study. The overall percentage of patients at goal blood pressure for Phase 2 was 89%. 75% of patients in Phase 1 were at goal. Patients on a single antihypertensive agent were at goal 91% of the time. Of those on multiple agents, 79% were at goal during Phase 2. Pharmacy compliance assessments were performed and the percentage of patients with blood pressure measurements not a goal due to non-compliance averaged 39.4%. The most frequently utilized agents were diuretics (36.6%), CCBs (19.7%), β-blockers (14.4%), and ACE-Is (14%).
CONCLUSIONS: Following aggressive management and adjustment of medications, blood pressures at goal improved in frail elders with hypertension. Hypertensive management in the PACE setting was successful due to pharmacist and primary care interventions.

Health Services Research/Managed Care

80. Targeting pharmacy errors to improve patient safety: a report from the ASIPS collaborative. *Laura B. Hansen, Pharm.D., BCPS,* David R. West, Ph.D., Daniel Harris, Ph.D., Douglas Fernald, M.A., Jack Westfall, M.D., Wilson Pace, M.D.; University of Colorado Health Sciences Center, Denver, CO; CNA Corporation, Alexandria, VA.

PURPOSE: Applied Strategies for Improving Patient Safety (ASIPS) collects and analyzes medical error data through a voluntary reporting system implemented in two Colorado Practice-Based Research Networks. These networks include 34 primary care practices involving over 470 clinicians and staff. Pharmacy errors have been identified in ~20% of more than 600 reports, with most involving the wrong drug, wrong dose/frequency, prescription/communication error, or lack of appropriate drug.
METHODS: A pharmacy-learning group, consisting of pharmacists, physicians, nurses, and research staff formed to develop practical interventions that address pharmacy error events reported to ASIPS.
RESULTS: Diagrams of process flow and typology of medication error events were developed to identify areas of potential pharmacy errors and help the learning group describe threats to patient safety and propose interventions to mitigate threats. Focus areas were based on likelihood of events, potential severity, and amenability to intervention. Threats included communication issues, delayed pharmacy processes, prescribing errors and use of drug samples. Possible mitigations included placing "virtual" pharmacists in practices, eliminating or developing "best practice" guidelines for samples, using preprinted prescriptions, discouraging "use as directed" for prescription instructions and encouraging electronic medical records with drug databases. The pharmacy-learning group prioritized threats and possible mitigations, will present them to the ASIPS Clinical Steering Committee and will implement selected interventions in primary care practices.
CONCLUSIONS: Identification and correction of pharmacy errors is critical to improve patient safety in primary care. The method described here will help practitioners develop interventions that are relevant to medication errors in their practices.

81. Osteoporosis risk is not limited to elderly Caucasians: findings from bone density screenings in Georgia. *John T. Johnson, Pharm.D.,* Jennifer L. Phillips, Pharm.D., Shashank B. Shinde, M.S., M.B.A., Ph.D. candidate; University of Georgia, Athens, GA.

PURPOSE: To determine if populations that are considered "low risk" for developing osteoporosis are at risk and to find out potential contributing factors for these results.

METHODS: Bone density screenings were performed on over 7000 men and women in Georgia between August 2001 and May 2003 with 6725 of these results having complete data. Questions asking individuals if they had received a prior bone density screening or test, current hormone replacement therapy, current smoking status, and knowledge and actual consumption of recommended daily calcium intake were collected.
RESULTS: Out of the 1058 African Americans screened, 76.9% were not consuming the recommended daily allowance of calcium and 89.8% had never had a previous bone density screening. Risk categories for developing a future fracture were based on T-scores with > 0 being defined as low risk, (-0.1 to -1.4) defined as moderate risk and a T-score < -1.5 defined as high risk. Of the African Americans < than 65 years old and > 65, 42.1% and 70.8% had T-scores in the moderate to high-risk range respectively. Men over the age of 65 were in the moderate to high risk 72.8% of the time. This compares to 57.3% of all patients screened younger than 65 and 80.2% of those older than 65.
CONCLUSIONS: Risk of a future fracture from osteoporosis can increase when patients are not aware of and do not follow preventative measures. Educating patients about prevention of osteoporosis is needed. "Low risk groups" should receive screenings for bone density to identify patients at risk so that prevention and/or treatment can be implemented.

Hematology/Anticoagulation

82. The influence of new amino acid complex of lithium on post-irradiation regeneration of hemopoiesis in experiment. *Louiza N. Zaljalutdinova, M.D.,* Rofia K. Khafizianova, M.D., Nailya E. Bakirova, P.D, Oleg A. Jadukov, Rafis M. Imanaev, P.D.; Kazan State Medical University, Russia; Kazan State Technological University, Russia.

Lithium carbonate is used for correcting some hereditary and gained neutropenias, in particular, at leukocytopenia at oncologist's patients after radiotherapy however its using not always effectively and is accompanied side effects. Organic ligands allow vastly to reduce toxicity of metals, as well as modulate their biological action. The role of separate amino acids in process hematopoiesis is noted and all this defines actuality of searching of potential stimulatories of hematopoiesis among complexes compounds of lithium with amino acids.
PURPOSE: The aim of our investigation was study the influence of a new amino acid complex of lithium on hemopoiesis at rats, which were exposed by total-body irradiation. The compound was created in chemical laboratory of Kasan State University
METHODS: The estimation an effect of new compound realized on model a total-body irradiation of rats, caused by total-body gamma-irradiation in dose 4,5 Gy on installation AGAT-R1. The rats has been receiving lithium intraperitoneal in dose 15 mg/kg since the third day after irradiation. The condition a hemopoiesis value on indexes of blood, hematopoietic marrow at rats in control group and experimental group before and after treatment. The results were processed statistical, using *t* criterion Student.
RESULTS: Results demonstrated that the treatment compound lithium accelerated post-irradiation recovery of hematopoietic marrow and corrected the indexes of blood at rats in experiment. Discovered increase the amount of monocytes in the treatment with new amino acid complex lithium post-irradiation, allows to expect that effect of compound realizes through interleukin-2, granulocyte-macrophage-colony-stimulating factor, selected macrophages or monocytes of microenvironment of bone-marrow, since they in sufficient degrees resistant to action of irradiation. Efficient recovery erythropoiesis in using the new compound of lithium can be explained as well as ability an to macrophages synthesize erythropoietin. New amino acid complex lithium shows pharmacological action after post-irradiation oppression hemopoiesis in total dose, corresponding 1/17 DL_{50} then as of literature, lithium carbonate - in DL_{50} , but lithium succinate - in 2/5 DL_{50}.
COUNCLUTION: Thereby, new amino acid complex lithium corrigens the syndrome post-irradiation myelosuppression at rats.

83. Update of stroke outcomes following implantation of the CardioWest total artificial heart. *Paul E. Nolan, Jr., Pharm.D.,* Francisco A. Arabia, M.D., Richard G. Smith, MSEE, Gulshan K. Sethi, M.D., Raj K. Bose, M.D., Pei H. Tsau, M.D., Mary E. Banchy, R.N., M.B.A., Daniel S. Woolley, M.D., Birger E. Rhenman, M.D., Michael S. McCarthy, B.A., Jack G. Copeland, M.D.; University of Arizona; University Medical Center, Tucson, AZ.

PURPOSE: To prevent postoperative cerebral vascular accidents (CVAs) following implantation of the CardioWest total artificial heart (CWTAH), which is under investigation as a bridge to cardiac transplantation, we use multi-system monitoring (MSM) to individualize a multi-drug regimen (MDM) consisting of unfractionated heparin, followed by conversion to warfarin, plus aspirin, dipyridamole and pentoxifylline. This describes the CVA outcomes at our institution following implantation with the CWTAH.
METHODS: Each patient's age, gender, implant time plus mean (± SD), median, range and pooled total implant times, and occurrence of postoperative CVAs were prospectively entered into a dedicated computerized database and results analyzed retrospectively. A CVA was defined as a prolonged (>72 hours) neurological deficit not present at baseline as determined by a standard neurological examination.
RESULTS: Between September 30, 1994 and July 23, 2002, 60 patients, 51 males (85%) and 9 females (15%), were implanted with the CardioWest TAH. The pooled total, mean (± SD), median and range of implant days were 5436 (14.89 years), 90.6 ± 92.3, 58, and 1 to 413 days, respectively. Postoperatively CVA occurred in one patient at 11-weeks post-implant resulting in an annualized rate for postoperative CVAs of 0.067 CVAs/patient-year.
CONCLUSIONS: At our institution the use of MSM to establish an individualized MDR following implantation of the CWTAH results in a very low postoperative CVA rate. The observed CVA rate is comparable to that in patients with non-valvular atrial fibrillation and following implantation of the HeartMate vented electric ventricular assist device or Medtronic Hall prosthetic valves.

84. Effect of direct thrombin inhibitors: bivalirudin, lepirudin, and argatroban, on prothrombin time measurements. *Robert C. Gosselin, C.L.S.,* William E. Dager, Pharm.D., Jeffrey H. King, Pharm.D., Kim A. Janatpour, M.D., Kathleen A. Mahackian, Pharm.D., Edward C. Larkin, M.D., John T. Owings, M.D.; University of California, Davis Medical Center, Sacramento, CA.

PURPOSE: To determine whether direct thrombin inhibitors (DTIs) affect INR measurements, potentially complicating warfarin anticoagulation.
METHODS: Lepirudin, bivalirudin, or argatroban was added to pooled normal plasma (PNP) at concentrations of 0.1, 0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 µg/ml. PNP (for ratio calculations) and DTI-plasma was then tested using PT reagents (ISI) from Beckman Coulter [PT-Fibrinogen Recombinant (1.11), PT-Fibrinogen (1.87), PT-Fibrinogen HS (1.42), PT-Fibrinogen HS PLUS (1.15), RecombiPlasTin (0.97)]; BioMerieux [Simplastin (1.27)]; Dade Behring [Innovin (1.03), Thromboplastin C+ (1.86), Thromborel S (0.92)]; Pharmanetics [TAS PT-One (1.05)]; Stago International [Neoplastine (1.75), Neoplastine Plus (1.33)] and Trinity Biotech [ThromboMax (1.54), ThromboMax HS (1.07)].
RESULTS: The mean PT ratio (95% confidence intervals) pooling all reagent data:

µg/ml	aPTT ratio[1]	Lepirudin	Bivalirudin	Argatroban
0.1	1.25 (1.20-1.30)	1.03 (1.02-1.04)*	1.06 (1.04-1.08)	1.09 (1.07-1.11)
0.2	1.42 (1.35-1.49)	1.06 (1.04-1.08)*	1.09 (1.07-1.11)*	1.15 (1.12-1.18)
0.4	1.68 (1.61-1.74)	1.09 (1.07-1.11)*	1.15 (1.12-1.18)*	1.33 (1.26-1.40)
0.6	1.87 (1.79-1.94)	1.13 (1.10-1.16)*	1.23 (1.19-1.28)*	1.46 (1.36-1.56)
0.8	2.01 (1.91-2.11)	1.16 (1.12-1.20)*	1.27 (1.22-1.32)*	1.66 (1.54-1.78)
1.0	2.12 (2.06-2.19)	1.19 (1.15-1.23)*	1.34 (1.27-1.41)*	1.84 (1.70-1.98)
1.2	2.23 (2.18-2.28)	1.20 (1.16-1.24)*	1.39 (1.31-1.47)*	2.05 (1.88-2.22)

[1]Mean aPTT ratio using Actin FS (Dade Behring); * p<0.05 Dunn's method ANOVA on ranks to Argatroban ratios

At 1.2 µg/ml of drug, INRs ranged from 1.07-1.46 for Lepirudin, 1.21-1.92 for Bivalirudin, and 1.62-3.82 for Argatroban.
CONCLUSIONS: At therapeutic concentrations, Argatroban has a significant effect on PT ratios and INR measurements. At higher drug concentrations, the INR bias will be pronounced with higher ISI reagents.

85. Comparison of two point-of-care methods for monitoring direct-thrombin inhibitor anticoagulation. *Robert C. Gosselin, CLS,* William E. Dager, Pharm.D., Jeffrey H. King, Pharm.D., Kim A. Janatpour, M.D., Kathleen A. Mahackian, Pharm.D., Edward C. Larkin, M.D., John T. Owings, M.D.; University of California Davis Medical Center, Sacramento, CA.

PURPOSE: Direct-thrombin inhibitors (DTI) are used in patients requiring anticoagulation that are contraindicated to heparin. Monitoring DTI anticoagulation effects include aPTTs, Ecarin Clotting Times (ECT) and potentially a new method, Thrombin Inhibitor Management (TIM) (Pharmanetics, Morrisville, NC).
METHODS: Argatroban, Bivalirudin, and Lepirudin were added to pooled normal plasma to achieve concentrations of 0.1, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 7.0 and 8.0 µg/ml. Samples were then tested, in duplicate, on the TAS analyzer (Pharmanetics) using ECT and TIM cards.
RESULTS: There was no significant difference between duplicate testing for ECT and TIM cards (p=0.891 and p=0.958 respectively). Both ECT and TIM demonstrated strong linear correlation with increasing concentrations of lepirudin (r=0.997 and r=0.987 respectively); bivalirudin (r=0.977 and r=0.948 respectively) and argatroban (r=0.983 and r=0.967 respectively). The correlation coefficients between the ECT and TIM for each DTI were >0.988. The slope measurements from regression analysis between ECT and TIM methods for each DTI were 1.34 for argatroban, 1.24 for lepirudin, and 1.03 for bivalirudin. There was no statistical difference between the TIM and ECT measurements for the plasma samples containing bivalirudin.
CONCLUSIONS: There was a linear correlation between the ECT and TIM methods and drug concentrations of lepirudin, bivalirudin and argatroban. There was no statistical difference between the ECT and TIM measurement times in bivalirudin anticoagulated samples. The ECT and TIM would provide a point-of-care alternative to laboratory aPTTs for monitoring DTI

anticoagulation.

86. Evaluation of the use and outcomes of erythropoietic proteins for the treatment of chemotherapy-induced anemia in the university-affiliated ambulatory setting. *George Jaresko, Pharm.D.,* Gene Gibson, Pharm.D., Olaf Dominguez, M.S., Mike Bloomfield, Pharm.D., Jodi Fink, Pharm.D., Emily Stuntebeck, Pharm.D.; Ivy Tonnu, Pharm.D.; University of Southern California, Los Angeles, CA; University of Pennsylvania, Philadelphia, PA; Cleveland Clinics Foundation, Cleveland, OH; University of Michigan Hospital, Ann Arbor, MI.

PURPOSE: Limited information has been published on the relative use and efficacy of darbepoetin alfa (darbepoetin) and epoetin alfa (epoetin) in the university-affiliated ambulatory setting. The purpose is to compare the utilization and outcomes of treating chemotherapy-induced anemia (CIA) with erythropoietic proteins (EP) in the university-affiliated ambulatory setting.
METHODS: Five health systems participated in this national retrospective review study of adult patients with CIA who received 3-24 weeks of erythropoietic therapy beginning in 2002. Data collected during treatment included patient demographics, EP usage and laboratory data. Univariate testing was utilized.
RESULTS: Data from 392 patients were abstracted; 121 darbepoetin and 259 epoetin patients were analyzed. The most frequent starting regimen (% of total) was darbepoetin 200µg every 2 weeks (Q2W;73%) and epoetin 40,000U weekly (QW;86%). Darbepoetin and epoetin mean (SD) [p-value] baseline hemoglobin (g/dL) was 10.6 (1.7) vs 10.6 (1.5) [p>0.1] and maximum mean hemoglobin was 11.6 (1.5) vs 12.0 (1.4) [p>0.1]. Mean (SD) duration of therapy (weeks) for darbepoetin was 9.6 (5.5) and for epoetin was 9.5 (6.7). Only four patients had iron studies before or during the EP treatment period.
CONCLUSIONS: Darbepoetin 200 µg Q2W has been adopted as a standard in university-affiliated ambulatory setting oncology practice, and it is as efficacious as epoetin 40,000 QW for CIA. Measurement of iron stores appears underutilized in the management of CIA in the university-affiliated ambulatory setting.

87. A retrospective evaluation of the direct thrombin inhibitors at a tertiary-care hospital. *Marybeth Hayman, Pharm.D.,* David B. Crabtree, CPhT, M.S., Shewan Aziz, R.Ph., Ph.D., BCOP; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: This review evaluated the appropriateness, efficacy, safety and cost associated with prescribing direct thrombin inhibitors (DTI) at Eastern Maine Medical Center where three DTIs, Bivalirudin, Argatroban and Lepirudin have been added to the hospital formulary.
METHODS: Medical records of 45 patients who received DTI therapy between 10/01/01 and 09/30/02 were randomly selected and evaluated. Patient demographics, indication for use, organ dysfunction, duration of treatment, complication of therapy, duration of therapy and cost were assessed.
RESULTS: DTI therapy with Lepirudin and Argatroban was routinely administered as a treatment for heparin induced thrombocytopenia (HIT), heparin induced thrombocytopenia thrombosis syndrome (HITTS) and for patients with a history of HIT (42, 34, and 21% respectively). Thrombotic complications were more common in the lepirudin group compared with argatroban (53 vs 36% p=0.09). Two amputations in the lepirudin group were performed. In the presence of renal dysfunction, administered doses of lepirudin were often low . Prior to argatroban administration, 29% of patients did not have hepatic function assessed. Bleeding rates were low for both drugs. Duration of therapy and cost for treatment were similar for both drugs, 8days and $3,200 respectively. Bivalirudin was routinely administered in the catheterization-lab setting. No major bleeds were identified and average cost per treatment was $323.
CONCLUSIONS: To facilitate proper prescribing, dosing, duration and treatment of HIT and HITTS a pre-printed HIT/HITTS order-set incorporating lepirudin and argatroban will be developed and distributed. Bivalirudin prescribing will be restricted to the catheterization laboratory.

88. Safety of low-dose enoxaparin in thrombocytopenic stem cell transplantation patients. *Rami B. Ibrahim, Pharm.D.,* Midya M. Gumma, Pharm.D. candidate, Nikki Milan, Pharm.D., Lance Heilbrun, Ph.D., Jared Klein, M.D., Roger Dansey M.D., Muneer H. Abidi, M.D., Esteban M. Abella, M.D.; Harper University Hospital; Karmanos Cancer Institute; Wayne State University, Detroit, MI.

PURPOSE: Our previously published experience with the safe use of 40-mg subcutaneous enoxaparin once daily in a stem cell transplantation (SCT) patient during the thrombocytopenic period (platelets < 50,000 cells/mm^3) (Annals Pharmacother 2002; 36: 1478) is extended now to 14 SCT patients. The primary objective of this case series was to evaluate the safety of this approach in this patient population at risk of bleeding.
METHODS: SCT patients who were receiving enoxaparin in full dose owing to history of a thrombosis or who developed a peri-transplant thrombotic event were decreased to daily 40-mg subcutaneous enoxaparin when platelets fell below 50,000 cells/mm^3 . We retrospectively determined the incidence of bleeding during thrombocytopenia.
RESULTS: Fourteen adult SCT patients were treated from October 2001 through March 2003. Nine of these patients (64%) received autologous SCT while the remainder received allogeneic myeloablative SCT (n=2), non-myeloablative SCT (n=2) and priming chemotherapy (n=1). The median weight was 85 kg (range: 53-117 kg). Median duration of thrombocytopenia was 11.5 days (range: 5-115 days). Enoxaparin was given for a median of 7 days (range: 5-115 days). Generally, enoxaparin was held when platelets fell below 20,000 cells/mm^3. Only one episode of bleeding (7%) was documented for these patients (epistaxis occurring at a platelet count of 25,000 cell/mm^3). Median number of platelet transfusions was 4 (range: 0-32).
CONCLUSIONS: The presented data suggests that low-dose enoxaparin is safe in SCT patients who have a platelet count > 25,000 cells/mm^3 and who weigh > 55 kg. Given these favorable safety findings, a phase-II pilot study evaluating the efficacy of 40-mg enoxaparin in reducing the incidence of catheter-associated upper extremity deep venous thrombosis in SCT patients will be initiated.

89. Preventing sub-therapeutic anticoagulation with a weight-based heparin nomogram in the treatment of venous thromboembolism. *Alexander J. Ansara, Pharm.D.,* Paul P. Dobesh, Pharm.D., Joy R. Abu-Shanab, Pharm.D., Jason M. Enders, Pharm.D.; St. Louis College of Pharmacy, St. Louis, MO; St. Luke's Hospital, Chesterfield, MO.

PURPOSE: Clinical evidence has demonstrated that sub-therapeutic levels of anticoagulation in the setting of venous thromboembolism (VTE) result in suboptimal clinical outcomes. Weight-based heparin nomograms have been proven to reduce sub-therapeutic aPTTs. We hypothesized that despite a weight-based nomogram, a number of patients may receive suboptimal anticoagulation. We evaluated the effectiveness of a standardized weight-based heparin nomogram in achieving and maintaining therapeutic aPTT values.
METHODS: A retrospective review of medical records was conducted for patients with VTE between 7/01-1/03. Data was collected on patient demographics; number of aPTTs; aPTTs over, in, or under the therapeutic range; and length of stay (LOS).
RESULTS: We identified 95 patients appropriately treated with the nomogram. Patients had a mean age of 67 ± 18 years, weighed 78.2 ± 20.5 kg, and were 61% female. Despite using the nomogram, 70% of patients experienced one sub-therapeutic aPTT, and 22% of patients had two sub-therapeutic aPTTs within the first five aPTTs measured. Compared to patients without a sub-therapeutic aPTT, patients with one sub-therapeutic aPTT had more aPTTs (13 vs 9; p=<0.001) and a trend toward a shorter LOS (9 vs 7 days; p=0.087), while patients having at least two sub-therapeutic aPTTs also had more aPTTs (15 vs 9 aPTTs, p=<0.001) and longer LOS (10 vs 7 days, p=0.006).
CONCLUSIONS: Despite using a heparin nomogram, many patients do not maintain therapeutic anticoagulation. Sub-therapeutic anticoagulation leads to more aPTTs and longer LOS, which may increase the cost of care. One approach to minimize these findings would be to utilize low-molecular-weight heparin.

90. Evaluation of formulary conversion from epoetin to darbepoetin in a community hospital. *John A. Noviasky, Pharm.D.,* Emile Wassel, M.D., Tom Ryan, M.D., Jon Bushnell, R.Ph.; St. Elizabeth Medical Center, Utica, NY.

PURPOSE: Analysis was conducted to determine if formulary interchange from Epoetin (EPO) 40,000 units to Darbepoetin (DARB) 60µg resulted in change in patient outcomes.
METHODS: Retrospective review of patients receiving EPO or DARB.
RESULTS: While most patient characteristics were similar (reason for admission, percentage patients having invasive procedure), the EPO population contained about half as many diabetics and renal patients. Few patients (<30%) had iron or ferritin levels ordered. Twenty-four doses of DARB were administered resulting in more than $6000 in cost avoidance.

	Epoetin (n=47) Mean(SD), Median	Darbepoetin (n=14) Mean(SD), Median
Age (years)	76.5 (8.4)	71.7 (11.7)
BMI	28.1 (7.9)	34.3 (9.5)
LOS (days)	16.1 (23.9), 11	20.7 (20.3), 12
Doses Received	1.5 (0.7)	1.7 (1)
Dose Received After Admission (Days)	5.9 (9.1)	7.2 (7.6)
Time from 1st Dose to Discharge (Days)*	10.5 (16.5), 6	13.5 (16.3), 6.5
Hematocrit Prior to Dose	30 (4.1)	28.7 (1.4)
Hematocrit After Dose**	32.3 (4)	30.1 (3)
Hematocrit Change (%)**	9 (18.5), 9.1	4.3 (11.7), 6.6
Units Blood Transfused Prior to Dose	1.6 (2.1), 1	3.1 (5.3), 1.5
Units Blood Transfused After Dose	0.6 (1.3), 0	1.3 (2.3), 0

*First Dose Given ≤ 1 Day Prior to Discharge (n,%) EPO(14,30), DARB (3,21); **n=21 EPO, n=6 DARB

CONCLUSIONS: It appears that interchange from EPO to DARB has not made appreciable change in patient outcomes. While some variables appear to favor EPO, small sample size and patient characteristics may account for difference. Data collection for DARB continues and guidelines should be considered for lab value (iron, ferritin) measurement.

91E. A assessment of an antibiotic treatment algorithm for chemotherapy-induced febrile neutropenia: physician acceptance and patient outcomes. *Christine K. Howe, B.S., B.Sc.Pharm.,* Linda D. Dresser, B.Sc.Pharm., Pharm.D., Allison J. McGeer M.Sc., M.D., FRCPC; Mount Sinai Hospital, Toronto, ON, Canada.

Presented at the Annual General Meeting of the Canadian Society of Hospital Pharmacists', St. John's NF, Canada, August 17-19, 2003.

92. Assessment of periprocedural anticoagulation management including the use of phytonadione. *Alicia M. Reese, Pharm.D., BCPS,* Lisa E. Farnett, Pharm.D., Cassandra S. Navarrete, P.A.C., Henry I. Bussey, Pharm.D., FCCP, Roger M. Lyons, M.D., FACP; Anticoagulation Clinics of North America, San Antonio, TX.

PURPOSE: Perioperative management of anticoagulation is a commonly encountered challenge. However, littler literature is available on which to formulate evidence-based recommendations or establish clinic protocols. In this study, we characterized and evaluated the method currently used at our private referral-based anticoagulation clinic for management of patients on warfarin therapy before and after planned invasive procedures.
METHODS: This retrospective cohort study used medical record data of patients who required interruption of chronic warfarin therapy for an invasive procedure between May 1, 2002 and April 30, 2003. Procedures were included only if the patient was managed entirely by clinic staff prior to the procedure. Primary outcomes were perioperative hemorrhagic and thrombotic events and achievement of the target INR for the procedure. Secondarily, we evaluated the rate of INR decline and the efficacy and safety of anticoagulation reversal with phytonadione.
RESULTS: We identified 134 procedures in 92 patients during the study period. The procedures with frequencies > 5% were endoscopies (39, 29.3%), cardiac biopsies (17, 12.8%), epidural injections (9, 6.8%), and cardiac catheterizations (7, 5.3%). Twenty-three patients had multiple procedures during the study period. Prior to the procedure, warfarin was suspended for a mean of 3.0 ± 1.2 days (range, 0 to 10 days), and an INR was obtained in clinic one day prior to and on the day of the procedure in 74.4% and 19.5% of cases, respectively. On the day prior to the procedure, 46 (46.5%) patients were ≤ 0.2 units above the procedure target, and 14 (53.8%) INRs on the procedure day were at the appropriate target. Phytonadione, low molecular weight heparins, and aminocaproic acid were used in 35.3%, 15.8%, and 8.3% of cases, respectively. For the majority of procedures (75.9%), patients restarted warfarin the evening following the procedure. Fifty-eight (43.6%) patients were no more than 0.1 units outside their therapeutic range at the post-procedure visit, with mean times to therapeutic range of 14.4 days and 1.8 clinic visits, respectively. There were 7 (5.3%) events of perioperative bleeding, 3 hematomas (1 epidural following vertebroplasty), 2 cases of rectal bleeding following colonoscopy, 1 case of epistaxis requiring hospitalization after esophagogastroduodenoscopy and 1 case of bleeding from a liver biopsy site. There were 2 (1.5%) thrombotic events, 1 DVT, and 1 TIA.
CONCLUSIONS: Overall, the management of perioperative anticoagulation in our clinic is safe and effective, but it could be improved. Using these data, a model procedure has been developed for periprocedural anticoagulation management that will be prospectively evaluated.

93. Correlation between antifactor Xa activity, thrombin generation time, platelet contractile force and clot elastic modulus following ex vivo enoxaparin exposure. *Donald F. Brophy, Pharm.D.,* Erika Martin, M.T. (ASCP), Todd W.B. Gehr, M.D., Marcus E. Carr, Jr., M.D., Ph.D.; Virginia Commonwealth University, Richmond, VA.

PURPOSE: Vigorous debate exists whether antifactor Xa activity is directly correlated to the degree of anticoagulation in patients receiving low-molecular weight heparin (LMWH). Thrombin generation time (TGT), platelet contractile force (PCF) and clot elastic modulus (CEM) are novel, global measurements of the integrity of the clotting system. The purpose of this study was to determine the correlation of antifactor Xa activity to TGT, PCF and CEM in healthy subjects.
METHODS: Eight healthy subjects provided whole blood samples that were spiked ex vivo with escalating doses of enoxaparin sodium (final antifactor Xa concentrations of 0.25, 0.50, 1.0 and 2.0 IU/ml). Mean TGT, PCF and CEM were then assessed at each antifactor Xa concentration. Antifactor Xa concentrations were determined using a validated aminolytic method. TGT, PCF and CEM were determined using the Hemodyne® hemostasis analyzer. Pearson's correlation was used to determine the relationship between antifactor Xa activity and TGT, PCF and CEM at each antifactor Xa concentration, using significance level $p \leq 0.05$.
RESULTS: For each ex vivo antifactor Xa concentration (including baseline), there was highly significant correlation between antifactor Xa and TGT (r=0.94, p=0.0179); PCF (r=-0.95; p=0.0144); and CEM (r=-0.97, p=0.0048).
CONCLUSIONS: The novel clotting measurements TGT, PCF and CEM are highly correlated to antifactor Xa activity when analyzed using an ex vivo enoxaparin model. Further in vivo studies are needed in patients to validate these findings, and to determine if TGT, PCF and CEM may provide more useful clinical information regarding the global anticoagulation status of patients receiving low-molecular weight heparin therapy.

94. Effect of experience with managing anticoagulant therapy on physician satisfaction with a pharmacist–operated anticoagulation clinic. *Jacqueline Super, Pharm.D.,* Ann K. Wittkowsky, Pharm.D., CACP, Emily Beth Devine, Pharm.D., M.B.A.; University of Washington, Seattle, WA.

PURPOSE: Dedicated anticoagulation services improve clinical outcomes in patients with warfarin, and are highly rated by referring physicians. This study evaluated physicians' satisfaction with a pharmacist operated anticoagulation clinic as a function of the physicians' level of experience with managing anticoagulant therapy.
METHODS: One hundred thirty-three physicians who referred patients to a university hospital-affiliated anticoagulation clinic system were surveyed. Survey questions were formulated to assess quality of care. Responses were stratified by implied level of physician experience with managing warfarin based on area of specialty practice. Cardiologists and hematologists/oncologists were compared to general medicine practitioners and other medicine specialties. Pearson Chi-square tests were used to evaluate the physician responses.
RESULTS: Surveys were returned by 78 (59%) of the surveyed physicians. Overall, physicians agreed that when managed by the anticoagulation clinic, patients experienced improved INR control(91%) and lower rates of adverse clinical events (63%), drug interactions (82%), warfarin-related ER visits (67%) and warfarin-related hospitalizations (64%). Eighty-eight percent of cardiologists and oncologists were very or moderately experienced with warfarin management compared to only 74% of general practitioners. However, no difference in any satisfaction variable was evident in comparing these two groups.
CONCLUSIONS: All satisfaction outcomes were highly rated by referring physicians. However, experience with warfarin management did not influence overall satisfaction with the care provided by the anticoagulation clinic.

95. Frequency and causes of over- and underanticoagulation in patients taking warfarin. *Ann K. Wittkowsky, Pharm.D.,* E. Beth Devine, Pharm.D.; University of Washington, Seattle WA.

PURPOSE: Warfarin therapy is influenced by numerous variables that can alter anticoagulant response. Frequent INR monitoring and warfarin dosing adjustments are required to prevent over- and underanticoagulation and associated adverse clinical events. The purpose of this investigation was to document the frequency and specific causes of over- and underanticoagulation in patients taking warfarin.
METHODS: The medical and anticoagulation clinic records of patients taking warfarin during a 12 month index period, and who were managed by a university-affiliated anticoagulation clinic, were evaluated retrospectively. At each clinic visit, pharmacist practitioners documented the most likely cause of over- or underanticoagulation based on patient examination and evaluation.
RESULTS: During a single year, 1020 patients, representing 668 pt-years of therapy, had 12,912 anticoagulation clinic visits. The frequency of underanticoagulation (INR < 2) was higher than the frequency of overanticoagulation (INR > 4) [24.8% vs 4.7%]. Drug interactions more commonly caused overanticoagulation than underanticoagulation [10.3% vs 3.3%], and accounted for only a small percentage of out-of-range INRs. Similarly, dietary, alcohol and disease state interactions were more frequently associated with overanticoagulation (24.7% vs 11.76%). Noncompliance was more likely to be associated with underanticoagulation (16.3% vs 5.6%), as was initiation therapy (15.6% vs 5.0%). Despite thorough patient evaluation, the most common source of both over- and underanticoagulation was indeterminate (42.3% vs 29.7%).
CONCLUSIONS: Out of range INRs are encountered frequently during warfarin therapy as a result of numerous factors. Often, no cause is apparent despite detailed assessment. When over- and underanticoagulation are encountered, adverse clinical outcomes may be prevented by cause-specific adjustments to both warfarin dosing and frequency of follow up.

96E. Clinical outcomes and medical resource utilization in patients with and without malignancy treated with warfarin. *Ann K. Wittkowsky, Pharm.D.,* David Veenstra, Pharm.D., Ph.D., David Blough, Pharm.D.; University of Washington, Seattle WA.

Presented at the XIX Congress of the International Society of Thrombosis and Haemostasis, Birmingham United Kingdom, July 16 2003.

97. The associated between age and INR in patients with warfarin-related major bleeding complications. *Kelly Whitely, Pharm.D.,* Ann K. Wittkowsky, Pharm.D., E. Beth Devine, Pharm.D., Edith Nutescu, Pharm.D.; University of Washington Medical Center, Seattle, WA; University of Washington, Seattle WA; University of Illinois, Chicago IL.

PURPOSE: The risk of major bleeding associated with warfarin increases with increasing INR. Advanced age has also been documented as an independent risk factor for warfarin-related hemorrhage. The purpose of this investigation was to evaluate the association between age and INR in patients with major bleeding events related to anticoagulation with warfarin.
METHODS: The medical and anticoagulation clinic records of patients on warfarin during a 19 month index period, and who were managed by two university-affiliated anticoagulation clinics, were evaluated retrospectively. Patients who experienced major bleeding, defined as bleeding requiring hospitalization, were included in the analysis. Multiple linear regression was used to evaluate associations, and t-testing confirmed results.
RESULTS: Sixty six patients (mean age 61.2 years; age range 21-90) who experienced major bleeding during the index period were evaluated. In patients ≥ 65 years of age, mean INR at the time of a major bleeding event was significantly lower than in patients < 65 years old (3.2 vs 4.2; p=0.017). For every increase in age by one year, there is a decrease in mean INR at the time of a major bleeding event by 0.03 units (p=0.021). Concomitant use of antiplatelet agents (including nonsteroidal anti-inflammatory agents) (p=0.913) and low molecular weight heparins (p=0.331) did not influence INR at the time of major bleeding.
CONCLUSIONS: Older patients experience warfarin-related major bleeding events at lower INRs than younger patients. Patients older then 65 may require more aggressive management of overanticoagulation to minimize the risk of major bleeding.

Herbal Medicine

98E. An assessment of the utilization of complementary and alternative medication in women with gynecologic or breast malignancies. *Marisa A. Navo, Pharm.D.,* Laura Michaud, Pharm.D., BCOP, Kellie Jones, Pharm.D., Diane C. Bodurka, M.D., J. Lynn Palmer, Ph.D., Karen Basen-Enquist, Ph.D., Gabriel N. Hortobagyi, M.D., John Kavanagh, M.D., Judith Smith, Pharm.D., BCOP; M.D. Anderson Cancer Center, Houston, TX.

Presented at the Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 31, 2003.

HIV/AIDS

99. Clinical application of therapeutic drug monitoring of antiretrovirals. *Judianne C. Slish, Pharm.D.,* Linda M. Catanzaro, Pharm.D., Lori D. Esch, Pharm.D., Francesco O. Lliguicota, B.S., Robin DiFrancesco, M.B.A., Ross Hewitt, M.D., Gene D. Morse, Pharm.D.; University at Buffalo; Erie County Medical Center, Buffalo, NY.

PURPOSE: 1) To examine the feasibility of real-time therapeutic drug monitoring (TDM) of antiretrovirals (ARV) in a clinical setting, identify possible causes of virologic failure, calculate inhibitory quotients (IQ), and examine concentrations during suspected drug toxicities. 2) To determine if TDM combined with HIV phenotyping can provide patient-specific IQs that may be useful to optimize salvage regimens.
METHODS: A web-based mechanism has been established for collection of plasma samples and reporting ARV concentrations. Twenty-three trough concentrations from 16 samples were collected between 11/2002 and 4/2003 and assayed by HPLC. ARV dosing regimens, concurrent medications, adherence and toxicity information, concomitant disease states, resistance, and laboratory data were acquired. Samples with phenotypic assays were used to calculate IQs for protease inhibitors including amprenavir, indinavir, lopinavir, nelfinavir, and saquinavir.
RESULTS: Of the 23 concentrations, 14 were obtained during virologic failure. Of these 14, 10 had viral loads high enough to obtain a phenotype. Eight of these had available phenotypes for IQ calculation ranging from 0.101 to 9.78. Fourteen ARV concentrations were within the range of previously reported trough data; seven were below and two were above. Factors contributing to unexpected trough concentrations included drug interactions, suboptimal dosing, non-adherence, hepatitis C coinfection, and malabsorption. Dose-adjustments were considered in four patients.
CONCLUSIONS: IQs observed in patients failing their current ARV regimen demonstrated levels of resistance that may be too high to overcome with dose adjustments. Clinicians should consider using TDM earlier in the course of treatment, obtaining ARV concentrations with HIV phenotypes to guide therapy.

100E. Antiretroviral medications and neuropsychiatric assessments in pediatric patients with human immunodeficiency virus. *Joshua Caballero, Pharm.D.,* Sandra Benavides, Pharm.D., Katalin Koranyi, M.D., Michael Brady, M.D., Milap C. Nahata, Pharm.D., M.S.; Ohio State University; Children's Hospital, Columbus, OH.

Presented at the 5th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, Paris, France, July 8-10, 2003.

Infectious Diseases

101. Antibiotic prophylaxis for prevention of wound infections after gastric bypass. Michelle Lee, Aileen Quach, Eliza Suen, Anh Tran, Jeffrey King, *John Siepler, Pharm.D., BCNSP,* Mohammed Ali, Bruce Wolfe; University of California Davis Medical Center, Sacramento, CA.

Purpose: Prophylactic antibiotics (ABX) are often used to prevent wound infections (WI) following Gastric bypass (GB). We designed an evaluation to determine the factors that affect WI following GB.
Methods: This evaluation was approved by the IRB at UCDMC. The charts for 184 consecutive patients receiving GB before Feb 2003 were reviewed. Data collected included: BMI, ABX given, type of and duration of operation, and wound infection. Cross tabulation and a logistic regression model were used to determine the risk of WI and significance of variables of interest.
Results: 184 patient charts were available. The mean weight was 157 kg, mean BMI was 53kg/M^2. Most (81%) received an open gastric bypass. 181 patients (98.4%) received a preoperative ABX dose. Post operative ABX were given to 133 (72%), thus 28% of the patients received no postoperative prophylaxis. 15 patients (8.3%) developed post-surgical WI (OR: 1.587, 95%CI: 0.498-5.387). BMI, type of operation, presence of DM, choice of or use of ABX for post op prophylaxis did not affect the incidence of WI. There was a correlation of wound infection with duration of operation (p = 0.04, 95% CI 3.4-3.74).
Conclusion: We demonstrated that antibiotic choice, operation choice, body mass and DM did not influence the incidence of WI following GB. Duration of operation correlated with incidence of WI. The incidence of WI in the 28% of patients who received no post operative ABX was almost identical to those who received antibiotics. Further work is needed in this area.

102E. Clinical and economic outcomes of a meropenem dosing protocol based on pharmacodynamic concepts. *Srividya Kotapati,* Joseph L. Kuti, Charles H. Nightingale, David P. Nicolau; Hartford Hospital, Hartford, CT.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

103. Patient tolerability of an intravenous immunoglobulin product (IVIG) manufactured without cold-ethanol precipitation and solvent-detergent extraction. *Jennifer Maurer, Ph.D.,* Kim Hanna, M.S., the IGIV-C Study Group; Bayer Pharmaceuticals Corporation, West Haven, CT; Bayer HealthCare, Research Triangle Park, NC.

A novel IVIG (IGIV-C; Gamunex(TM), 10%), manufactured using an innovative, integrated caprylate and chromatography-based method, has eliminated alterations in structure and function of human IgG induced by cold-ethanol precipitation and solvent-detergent extraction. As the new process results in improved product purity, clinical experience should reflect improved product tolerability.
PURPOSE: This current analysis evaluates tolerability of IGIV-C during and 24 hours post infusion as compared to a licensed IGIV-SD (Gamimune® N, 10%) in adult and pediatric patients (<18 years of age).
METHODS: Clinical data were collected in multicenter, randomized, double-blind, parallel group studies comparing IGIV-C (n=135) to IGIV-SD (n=134) for therapy of primary immune deficiency (PID; ≤600 mg/kg monthly, for 9 months) or idiopathic thrombocytopenic purpura (ITP; 1 gm/kg/day, for 2 days). Premedication with steroids to alleviate infusion-related adverse events (AEs) was not allowed. AEs on study were recorded and rated by the investigator as to severity and relationship to study drug.
RESULTS:

Population	Incidence of Drug-related AEs per Infusion (%)					
	Any		Serious		Severe	
	IGIV-C	IGIV-SD	IGIV-C	IGIV-SD	IGIV-C	IGIV-SD
All Pediatric Patients	7.79	9.47	0.00	0.59	0.00	0.30
All Adult Patients	9.17	9.76	0.59	0.32	1.48	1.28

The most frequently occurring severe or serious AE was headache. No drug-related thrombotic events were observed in this analysis.
CONCLUSIONS: As both products used are liquid-formulated with glycine, hyperosmolality AEs that may be associated with sugar formulations have been avoided. These clinical data show that IGIV-C is at least as well tolerated as IGIV-SD, and the excellent tolerability may be a reflection of the innovative production process.

104. Influence of granulocyte colony-stimulating factor on treatment of *Pseudomonas aeruginosa* pneumonia in non-neutropenic host. *Chinedum P. Babalola, Ph.D.,* Charles H. Nightingale, Ph.D., David P. Nicolau, Pharm.D. FCCP; Center for Anti-Infective Research and Development; Hartford Hospital, Hartford, CT.

PURPOSE: Pretreatment with granulocyte colony-stimulating factor (G-CSF) has been shown to have direct effects on proliferation and bactericidal activities of neutrophils. It has been demonstrated recently that in neutropenic host, adjunctive treatment with G-CSF markedly enhanced the survival of mice already infected with *Pseudomonas aeruginosa* (PSA)

pneumonia. The aim of this study was to determine whether G-CSF could be beneficial as an adjunct to ceftazidime (TAZ) in treatment of the same infection in non-neutropenic host.
METHODS: Pneumonia was induced in Swiss Webster female mice (20–25g) by intratracheal instillation of $5x10^9$ CFU of PSA. Dose ranging studies were undertaken with TAZ and G-CSF via the SC route. Two hours after inoculation, the animals received either saline, G-CSF (150 µg/kg or 300 µg/kg) x 3 days, TAZ 2000 mg/kg x 2 doses or a combination of G-CSF and TAZ. Survival was monitored at different time points for 5 days.
RESULTS: Survival was markedly better in the groups that received TAZ alone or TAZ + G-CSF combination than in control or G-CSF alone ($p<0.05$). Survival in mice treated with TAZ + G-CSF was not significantly different from those treated with TAZ alone (30% vs 43%, p=0.6116 with 150 µg/kg G-CSF and 20% vs 9%, p=0.202 with 300 µg/kg G-CSF).
CONCLUSIONS: The adjunctive treatment with G-CSF to therapy with ceftazidime after onset of *Pseudomonas aeruginosa* pneumonia may not be beneficial to non-neutropenic host.

105. In vivo pharmacodynamic characterization of meropenem and its impact on the selection of resistance among *Pseudomonas aeruginosa*. *Christine T. Ong, Pharm.D.,* Pamela Tessier, M.S., Chonghua Li, Ph.D., Charles H. Nightingale, Ph.D., David P. Nicolau, Pharm.D.; Center for Anti-infective Research and Development, Hartford, CT.

PURPOSE: This study was designed to characterize the pharmacodynamic (PD) (%T>MIC) of meropenem (MER) and its impact on the selection of resistance against *Pseudomonas aeruginosa* (PSA).
METHODS: Mice were rendered neutropenic and inoculated with 106 CFU/thigh. MER pharmacokinetics (PK) were determined using doses of 50-300 mg/kg. PA01 (wild type strain) and K119 (expressing MexAB-OprM) were utilized. MICs were determined by broth microdilution and agar techniques. MER was administered to produce various %T>MIC over 24 hours. Bactericidal activity was assessed by the change in log CFU and the E_{max} model was applied to characterize PD. Samples were inoculated onto MER containing agar plates for bacterial subpopulation analysis.
RESULTS: MER exhibited linear PK over the doses studied. Comparable MICs were obtained for both agar and microdilution techniques with median values of 0.25 (PA01) and 0.125 µg/ml (K119). At ≥30% T>MIC, maximal kill was observed (PA01, 2.73-2.89 log CFU; K119, 1.12-1.51 log CFU) and resistant subpopulations did not emerge. While kill was scant at exposures of <20% T>MIC, only <0.5% of these organisms grew on plates containing MER at 2x MIC.
CONCLUSIONS: While the magnitude of bactericidal activity appeared different between the isolates it was achieved with similar MER T>MIC (30-40%). While MER exposures were studied over a wide range, little if any selection of resistance was noted even when doses were suboptimal. These data suggests that the in vivo emergence of PSA resistance should be minimized in man since commonly utilized doses result in exposures of >30% T>MIC for susceptible PSA.

106E. Relationship of intravenous immune globulin (IGIV) composition, dosing and infection prophylaxis. *John Strell, R.Ph.,* Erwin Gelfand, M.D., Kim Hanna, M.S., the IGIV-C in PID Study Group; Bayer HealthCare, West Haven, CT; National Jewish Medical and Research Center, Denver, CO; Bayer HealthCare, Research Triangle Park, NC.

Presented at the Annual Meeting of the Federation of Clinical Immunology Societies, Paris, France, May 15-19, 2003.

107. Incidence of methicillin-resistant *Staphylococcus aureus* expressing inducible clindamycin resistance in a community hospital. Robert C. Jerris, Ph.D., *Julie A. Hixson-Wallace, Pharm.D., BCPS*; Mercer University, Atlanta, GA; DeKalb Medical Center, Decatur, GA.

PUPPOSE: Susceptibility testing of many methicillin-resistant *Staphylococcus aureus* (MRSA) isolates reveals sensitivity to clindamycin and resistance to erythromycin. This profile is most often the result of the presence of the *erm* gene. The *erm* gene encodes enzymes that methylate the 23S rRNA. Expression of the *erm* gene may be constitutive or inducible. Standard susceptibility methods readily identify constitutive strains, but not inducible ones. Inducible isolates can rapidly develop clindamycin resistance in vitro, which may have in vivo importance. This study documented the incidence of inducible clindamycin resistance in MRSA isolates in a community hospital.
METHODS: MRSA isolates testing susceptible to clindamycin and resistant to erythromycin on the Vitek 2 system (bioMerieux) were selected for further susceptibility evaluation. A disc diffusion method was used to induce and detect resistance to clindamycin. A 0.5 McFarland inoculum of organism was streaked onto Mueller-Hinton agar plates. Erythromycin and clindamycin discs were placed on the plates at a distance of 12 mm apart. The plates were incubated overnight in ambient air at approximately $35^{B}C$. The zone of inhibition around the clindamycin disc was examined for a blunted response on the side nearest the erythromycin disc. Presence of a blunted response indicated induction of clindamycin resistance.
RESULTS: Twenty-five isolates fitting the susceptibility profile have been subjected to further testing. Of these isolates, 48% expressed inducible clindamycin resistance.
CONCLUSIONS: The presence of inducible clindamycin resistance is fairly common in our MRSA isolates. This information can be useful in guiding antibiotic therapy for infections caused by these strains.

108. Evaluation of coagulase-negative staphylococcus bacteremia in a tertiary care hospital in North Carolina. *Rosemary Persaud, Pharm.D.,* James D. Whitehouse, M.D., M.S., John D. Phillips, Pharm.D.; Mission St. Joseph's Hospital, Asheville, NC; University of North Carolina, Chapel Hill, NC.

PURPOSE: This study evaluated coagulase-negative staphylococcus (CNS) blood cultures to determine 1) true bacteremia versus contamination, and 2) appropriateness of vancomycin use among physicians in treating CNS bacteremias.
METHODS: Retrospective chart review of 77 patients admitted between September 1 and October 30, 2002 was performed. Inpatients greater than 18 years old, with at least one positive CNS blood culture identified by microbiology, had the following reviewed: clinical presentation, serial blood cultures, antimicrobial therapy, and presence of a central-venous catheter. Diagnostic criteria for bacteremia developed by the CDC were used.
RESULTS: True bacteremia occurred in 19 (25%) of 77 patients; fourteen received appropriate treatment with vancomycin for a mean of 10 days. Fifty-six (97%) of 58 patients with single blood cultures were appropriately treated as contaminants. Fifteen (26%) of 58 contaminants received vancomycin for a mean duration of 2 days. Two patients who did not meet criteria for CNS bacteremia were treated inappropriately with vancomycin exceeding 72 hours. Only one vancomycin trough level was requested for patients with contaminants, therefore unnecessary costs were avoided.
CONCLUSIONS: Coagulase-negative staphylococcus remains a contaminant in the majority of positive blood cultures. Continued educational activities have led to improved assessment of single blood cultures for CNS and the judicious use of vancomycin.

109. Effect of Ensure on the oral bioavailability of gatifloxacin. Michael B. Kays, Pharm.D. BCPS, FCCP, *Brian R. Overholser, Pharm.D.,* Seema Lagvankar, D.O., Mitchell Goldman, M.D., Kevin M. Sowinski, Pharm.D., BCPS, FCCP; Purdue University; Indiana University, Indianapolis, IN.

PURPOSE: The purpose of this randomized, single-dose, crossover study was to determine the effect of Ensure on the relative oral bioavailability (F) of gatifloxacin (GAT) in healthy volunteers.
METHODS: Twelve subjects (6M, 6F) received GAT 400 mg PO with water or Ensure in random order (washout period ≥ 7 d). Subjects ingested 120 ml of study liquid (water or Ensure) every 30 minutes x 5 doses. With the second study liquid dose, subjects ingested a single GAT tablet that was uniformly crushed and mixed into the study liquid. The dose cup was rinsed with an additional 60 ml of study liquid to insure ingestion of the entire dose. Serial blood samples were collected for 48 h, and GAT serum concentrations were determined by HPLC. Pharmacokinetic (PK) parameters were determined by noncompartmental analysis, and the relative F of GAT was calculated as $AUC_{0-\infty,\ Ensure}/AUC_{0-\infty,\ water}$. Differences in PK parameters were determined by paired t-test or Wilcoxon signed rank test, where appropriate. A 10,000 subject Monte Carlo simulation was performed to estimate the probability of obtaining a free AUC/MIC ≥ 30 for GAT with water and Ensure against 4,738 *S. pneumoniae* isolates.
RESULTS: PK parameters (mean [± SD] or median [range]) are shown below.

	GAT + Water	GAT + Ensure	p-value
C_{max} (mg/ml)	4.35 (0.90)	2.41 (0.58)	<0.0001
T_{max} (h)	1.0 (0.5-1.5)	2.5 (1.0-4.0)	0.006
Half-life (h)	7.9 (1.6)	8.2 (1.5)	NS
$AUC_{0-\infty}$ (mg*h/L)	42.4 (10.1)	31.3 (8.3)	<0.0001
Relative F	1.00	0.74 (0.12)	<0.0001

For *S. pneumoniae*, the target attainment rate was 99.2% and 98.5% for GAT with water and Ensure, respectively.
CONCLUSIONS: Ensure significantly decreases the C_{max}, T_{max}, $AUC_{0-\infty}$, and relative F of GAT, but the magnitude of these changes was not sufficient to alter the target attainment rate against *S. pneumoniae*.

110. Increasing fluoroquinolone and macrolide resistance with decreasing penicillin resistance among clinical isolates of *Streptococcus pneumoniae* from 1999 to 2002-2003. *Michael B. Kays, Pharm.D., BCPS, FCCP,* Gerald A. Denys, Ph.D., David W. Smith, Pharm.D., Matthew F. Wack, M.D.; Purdue University; Clarian Health Partners, Inc.; Methodist Hospital, Indianapolis, IN.

Based on a large national surveillance study, penicillin and azithromycin resistance among *Streptococcus pneumoniae* in the United States increased from 1999 to 2002 while levofloxacin resistance remained low (< 1%).
PURPOSE: To evaluate the in vitro activity and resistance rates over time for penicillin, macrolides, and fluoroquinolones against *S. pneumoniae* at our institution.
METHODS: MICs were determined by broth microdilution (NCCLS) for penicillin, azithromycin, clarithromycin, clindamycin, levofloxacin, gatifloxacin, moxifloxacin, and gemifloxacin against *S. pneumoniae* isolated

from January 1999 to December 1999 (n=170) and from January 2002 to April 2003 (n=150). All isolates were cultured from infected patients at our institution (>1,000 beds), and duplicate isolates were excluded. The MIC_{90} was calculated for each agent, and isolates were categorized as susceptible, intermediate, or resistant using NCCLS or FDA (gemifloxacin) breakpoint concentrations. Differences in resistance rates were determined by chi-square ($p<0.05$).
RESULTS: The MIC_{90} and resistance rates for 1999 and 2002-2003 are shown below:

	MIC_{90} (µg/ml)		Resistance (%)		
	1999	2002-2003	1999	2002-2003	p-value
Penicillin	2	2	22.4	16.0	0.151
Azithromycin	4	> 32	24.7	34.0	0.068
Clarithromycin	4	> 32	24.1	33.3	0.068
Clindamycin	0.06	> 32	5.9	12.0	0.053
Levofloxacin	1	2	0.6	4.0	0.037
Gatifloxacin	0.25	0.5	0.6	3.3	0.071
Moxifloxacin	0.12	0.25	0.6	3.3	0.071
Gemifloxacin	0.016	0.03	0.6	1.3	0.49

CONCLUSIONS: Penicillin resistance in *S. pneumoniae* decreased from 1999 to 2002-2003 while the MIC_{90} and resistance rates increased for the other agents tested, reaching statistical significance for levofloxacin. Although national surveillance studies provide important susceptibility information, these data demonstrate the importance of local susceptibility testing to identify and respond to changes in antimicrobial resistance.

111. Pharmacodynamic evaluation of garenoxacin, a novel des-F(6)-quinolone, compared to four fluoroquinolones against *Streptococcus pneumoniae* using Monte Carlo analysis. *Michael B. Kays, Pharm.D., BCPS, FCCP,* Gerald A. Denys, Ph.D.; Purdue University; Clarian Health Partners, Inc.; Methodist Hospital, Indianapolis, IN.

Garenoxacin (BMS-284756) is an investigational des-F(6)-quinolone that lacks the fluorine molecule at position 6 of the fluoroquinolone (FQ) structure. Like FQs, the pharmacodynamics of garenoxacin are best characterized by the AUC/MIC ratio.
PURPOSE: To compare the pharmacodynamic profiles of garenoxacin, levofloxacin, gatifloxacin, moxifloxacin, and gemifloxacin against *Streptococcus pneumoniae* using Monte Carlo analysis.
METHODS: MICs were determined by broth microdilution (NCCLS) for 150 clinical, non-duplicate isolates of *S. pneumoniae* cultured from infected patients at our institution between January 2002 and April 2003. The AUC (mean ± SD) for each agent was obtained from single dose studies in normal volunteers, and the percent protein binding utilized in the analysis was 75%, 30%, 20%, 52%, and 60% for garenoxacin, levofloxacin, gatifloxacin, moxifloxacin, and gemifloxacin, respectively. A 10,000 patient Monte Carlo simulation was performed to estimate the probability of achieving a target free AUC/MIC ratio ≥ 30 and ≥ 50 for garenoxacin 400 mg, levofloxacin 500 mg and 750 mg, gatifloxacin 400 mg, moxifloxacin 400 mg, and gemifloxacin 320 mg.
RESULTS: The MIC_{50}/MIC_{90} (µg/ml) were as follows: garenoxacin, 0.06/0.06; levofloxacin, 1/2; gatifloxacin, 0.25/0.5; moxifloxacin, 0.12/0.25; gemifloxacin, 0.016/0.03. The probability of achieving a free AUC/MIC ratio ≥ 30 and ≥ 50, respectively, was 97.6% and 96.6% for garenoxacin, 70.7% and 25.4% for levofloxacin 500 mg, 90.4% and 72.8% for levofloxacin 750 mg, 95.7% and 94.3% for gatifloxacin, 96.1% and 94.6% for moxifloxacin, and 96.4% and 94.4% for gemifloxacin.
CONCLUSIONS: Despite marked differences in the activity of these agents in vitro, target attainment rates for garenoxacin, gatifloxacin, moxifloxacin, and gemifloxacin were similar for these pneumococcal isolates. Target attainment rates for both levofloxacin doses were lower than the other agents, but the 750 mg regimen achieved the AUC/MIC targets more frequently than the 500 mg regimen.

112. Pharmacokinetics of once-daily aminoglycoside dosing in postpartum patients. *Mikael D. Jones, Pharm.D.,* John A. Armitstead, M.S., R.Ph., Kelly M. Smith, Pharm.D., Arthur T. Evans, M.D., George A. Davis, Pharm.D.; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Recent studies in postpartum patients with endometritis and/or chorioamnionitis found that once-daily dosing of aminoglycosides (ODA) had equivalent safety and efficacy as traditional dosing. However, pharmacokinetic data of ODA in postpartum patients are limited since serum concentrations were obtained during the distribution phase. The objective of this study was to characterize the pharmacokinetics of ODA in postpartum patients.
METHODS: Postpartum patients received gentamicin 5 mg/kg intravenous every 24 hours with ampicillin or clindamycin. Post-distributional serum gentamicin concentrations were obtained at 4 and 12 hours after the first dose. Pharmacokinetic parameters were calculated assuming a 1-compartment model using the Sawchuk-Zaske method. Data collection included duration of antibiotic therapy, duration of fever, and length of stay following initiation of antibiotics.
RESULTS: Nineteen postpartum patients (age, 25.6±5.5 years; weight, 79.6±19 kg) received 387±94 mg gentamicin. Duration of antibiotic therapy, 2.3±1.1 days; time to defervescence, 12.4±7.8 hours; and length of stay, 7.9±14.5 days. Thirteen patients had serum concentrations drawn appropriately. Pharmacokinetic parameters (mean ± SD) were:

	Concentration (µg/ml)
2-hour*	10.1 ± 3.4
4-hour	6.4 ± 1.8
12-hour	1.1 ± 0.3
24-hour*	0.08 ± 0.05
Ke ($hour^{-1}$)	0.22 ± 0.03
$t_{1/2}$(hours)	3.2 ± 0.5
V_d (L/kg)	0.33 ± 0.13
$AUC_{(0\text{-}24\ hours)}$ (µg/ml•hour)	74.8 ± 21.6

*Extrapolated concentrations

CONCLUSIONS: Extrapolated peak concentrations were lower than previous pharmacokinetic studies of ODA in postpartum patients. Mean $AUC_{(0\text{-}24\ hours)}$ was within the desired range of 70-100 µg/ml?h. Length of antibiotic therapy, fever, and hospital stay were consistent with previous studies. ODA is a reasonable dosing alternative in postpartum patients but the necessity of serum drug monitoring warrants further investigation.

113. Pharmacodynamic activity of free garenoxacin compared to ciprofloxacin, levofloxacin and ofloxacin vs *Streptococcus pneumoniae* using an in vitro pharmacodynamic model. *George G. Zhanel, Ph.D.,* Rhiannon Harris, B.Sc., Ayman Noreddin, Ph.D., Daryl J. Hoban, Ph.D.; University of Manitoba Health Sciences Center, Winnipeg, Manitoba, Canada.

PURPOSE: The pharmacodynamic (PD) parameter that best correlates with bacteriological eradication for fluoroquinolones (FQ) is the area under the serum concentration curve (AUC) to MIC (AUC/MIC) ratio. This study compared the PD parameters of garenoxacin (GRN), ciprofloxacin (CIP), levofloxacin (LEV) and ofloxacin (OFLO) against *S. pneumoniae* (SPN).
METHODS: Three strains of SPN were studied. MIC's of these strains were GRN 0.06 ug/ml, Cip 2 ug/ml, LEV 1 ug/ml and OFLO 2 ug/ml. The in virto pharmacodynamic model (IVPM) was inoculated with $1x10^6$ CFU/ml and each FQ was dosed to simulate free AUC_{24} and $t_{1/2}$ obtained after standard doses in healthy volunteers (GRN: 400 mg QD, AUC_{24} 20, $t_{1/2}$ 16 hours; CIP: 500 mg BID, AUC_{24} 14, $t_{1/2}$ 4 hours; LEV: 500 mg QD, AUC_{24} 35, $t_{1/2}$ 7 hours; and OFLO: 400 mg BID, AUC_{24} 39, $t_{1/2}$ 7 hours. Sampling was performed over 48 hours.
RESULTS: The following free (protein unbound) AUC_{24}/MIC ranges were simulated: GRN, 333; CIP, 7; LEV, 35; and OFLO, 19.5. GRN and LEV achieved free AUC_{24}/MIC ≥ 35, and all were bactericidal (≥ 3 log_{10} killing) with complete eradication by 12 hours and no regrowth at 24 or 48 hours. CIP and OFLO achieved free AUC_{24}/MIC =7 and 19.5, respectively and failed to achieve bactericidal activity at 12, 24 hours, and regrowth occurred at 48 hours. DNA sequencing of ParC and GyrA showed that CIP and OFLO regrowth strains were ParC mutants.
CONCLUSIONS: GRN and LEV were bactericidal at free AUCs that mimic human dosing. Both CIP and OFLO were associated with regrowth of *S. pneumoniae* with generation of ParC mutants.

114. Pharmacodynamics/pharmacogenomics of anti-mycotic combinations. *John D. Cleary, Pharm.D.,* Stanley. W. Chapman, M.D.; University of Mississippi, Jackson, MS.

PURPOSE: Our purpose was to evaluate anti-fungal drug combinations in an in vitro model to identify pharmacogenomic signatures that can be utilized as surrogate markers for drug toxicity.
METHODS: Our model utilizes human monocytic cells (THP-1; 3.0 x 10^7 cells/ml) to characterize hematopoietic and immunologic responses to anti-fungals. Cells were exposed for 0.5, 1, 2. 6 and 24 hours to Amphotericin B (AB) or AB Lipid Complex (ABLC) 5 ug/ml + 5-flurocytosine (5FC) 100 ug/ml, caspofungin (CAS) 20 ug/ml or media. Total RNA was used for cDNA synthesis/amplification, indirectly labeled with immuno-fluorescent tags (Cy3 or Cy5), then hybridized to a human cDNA micro-array containing 12,933 known transcripts or ESTs. The identity of specific transcripts with altered regulation (>1.5 fold) was performed using variable intensity analysis. Selected transcripts were validated using RT-PCR with unique primers.
RESULTS: Over time, a maximum of 1.3% and 18.4% of transcripts were up or down-regulated in response to anti-fungal combinations, respectively. The addition of 5FC to AB/ABLC significantly altered transcripts that regulate hematopoietic cell proliferation and homeostasis. This altered gene expression signature may reflect the hematopoietic toxicity observed clinically. 5FC also resulted in down-regulation of mercaptopyruvate sulfurtransferase that might mediate a drug interaction when AB formulations + 5FC are administered with nitroprusside. In contrast, AB appears to reverse the N-methyl-transferase inhibition caused by CAS. Down-regulation of this enzyme may be the cause of CAS infusion related reactions. Combination of AB + CAS may lead to less reactions than CAS alone.
CONCLUSIONS: These studies have identified a number of mRNA transcripts representing altered gene regulation associated with anti-mycotic

combination. Further clinical investigation is needed to elucidate pathways involved in human toxicity that correlate best with these in vitro observations.

115. Thrombocytosis associated with candidemia and its' treatment. Angela D. Saathoff, Stephanie Elkins, M.D., Stanley.W. Chapman, M.D., *John D. Cleary, Pharm.D.*; University of Mississippi, Jackson, MS.

PURPOSE: In this report, we describe a case series of thrombocytosis observed in patients treated for disseminated candidiasis.
METHODS: Candidemic patients (n=55) seen in consultation by Adult Infectious Diseases at a university medical center were selected for a retrospective chart review (8/1995 to 6/2003). A defined database was completed on each patient, including: demographics and concomitant diseases or medications. In addition, patients who received platelet administration and pharmacologic or pathologic contributors to thrombocytosis were stratified within groups. Secondary, "reactive", thrombocytosis was defined as a platelet count >400,000/mm^3 or a 2-fold increase from baseline.
RESULTS: Fifty-two percent of patients (71% men; 43% Caucasian) suffered reactive thrombocytosis. The average age (52 years), weight (83 kg) and frequency of known causes of thrombocytosis were not significantly different between reactors and nonreactors. In 86% of patients, an azole (voriconazole 6 mg/kg/d, 71%; fluconazole 6-12 mg/kg/d, 15%) was the only anti-fungal agent utilized. Likewise, the species of infecting Candida did not appear to affect the platelet count. Mean baseline platelet counts were 320,000/mm^3 with a mean peak (696,000/mm^3) occurring 11 days after initiation of therapy. The maximum peak (1,056,000/mm^3) was observed in one patient 14 days post-therapy initiation. Mean time to onset was 7 days and duration of thrombocytosis was 20 days post-therapy initiation.
CONCLUSIONS: The development of reactive thrombocytosis is worrisome due to the increased association with gastrointestinal tract bleeding and stroke. In this series, thrombocytosis was observed frequently during the treatment of candidemia. Whether associated with drug or pathogen will need to be elucidated by performing a controlled trial.

116E. Serial sinus aspirate sampling: a novel technique for evaluating antimicrobial therapy of acute maxillary sinusitis. *Paul G. Ambrose, Pharm.D.,* Ronald N. Jones, M.D., Scott Van Wart, Joel S. Owen, Mary Eileen C. McPhee, R.N., M.S., Chris Costanzo, Sujata M. Bhavnani, Pharm.D., Jack Anon, M.D.; Cognigen Corporation, Buffalo, NY; The Jones Group, North Liberty, IA; University of Pittsburgh, Pittsburgh, PA.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14–17, 2003.

117E. Relationship between increased levofloxacin use and decreased susceptibility of *Streptococcus pneumoniae*: report from the ARREST program. *Sujata M. Bhavnani, Pharm.D.,* Jeff P. Hammel, M.S., Ronald N. Jones, M.D., Paul G. Ambrose, Pharm.D.; Cognigen Corporation, Buffalo, NY; The Jones Group, North Liberty, IA.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14–17, 2003.

118. Use of meropenem in patients with a history of penicillin allergy. *Patrick J. Sommo, B.S., Pharm.D. candidate,* Ben M. Lomaestro, Pharm.D.; Albany Medical Center Hospital, Albany, NY.

PURPOSE: Patients requiring carbapenems frequently have a vague history of penicillin allergy. This investigation describes meropenem challenge in patients with a history of penicillin allergy.
METHODS: Medical records of patients prescribed meropenem between July 1, 2001 and August 1, 2002 in a large tertiary care teaching institution were reviewed. Penicillin allergies were ascertained and coded as either "self reported" via oral questioning of the patient or hospital medical record history, or "documented" through witnessing by a health care professional. Allergies were further sub-classified on the basis of specific reaction and as "likely allergic", "unlikely allergic", or "unknown".
RESULTS: 288 patients prescribed meropenem received a total of 365 courses. 58 (20%) patients with a history of penicillin allergy received 68 (19%) courses. Reactions were "self reported" in 67 patients and "documented" in one patient. Reactions included: rash (14), hives (5), itching (1), swollen neck and eyes (1), bruising (1), body edema (1) and unknown (44). No patient had a history of anaphylaxis. The documented reaction was a rash. Of the 68 treatment courses, two patients experienced a rash. These patients received 7 days and 2 days of meropenem.
CONCLUSIONS: Patients frequently are labeled as "penicillin-allergic". which limits their future treatment options. Greater care should be taken in obtaining the true nature of antimicrobial allergies. We were able to identify a large number of patients who required and received meropenem successfully despite a history of penicillin allergy. Patients with a history of anaphylaxis to penicillins or cephalosporins did not receive meropenem.

119. Streptokinase, but not tPA, improves survival in experimental sepsis. *D.P. Healy, Pharm.D., FCCP,* C. Leonard, B.S., M.B. Bottorff, Pharm.D., FCCP, A.N. Neely, Ph.D., I.A. Holder, Ph.D.; University of Cincinnati; Shriners Hospitals for Children, Cincinnati, OH.

BACKGROUND: The pathogenesis of sepsis is due to a loss of homeostasis between inflammation, coagulation and fibrinolysis. "Failed" agents were primarily antiinflammatory. The efficacy of activated protein C in sepsis is purportedly due to a combination of antiinflammatory, anticoagulant and fibrinolytic mechanisms.
PURPOSE: To determine if tPA or streptokinase (SK) improves survival in burned mice with sepsis and provide proof-of-concept data that fibrinolytic therapy is beneficial in sepsis.
METHODS: An established murine model of sepsis was used to produce a 15% TBSA non-lethal burn (J Endotox Res 1996;3:229). *K. pneumoniae* (10^3 cfu) given s.c. results in >90% mortality by day 5 post burn/infection (b/i). Saline, ceftazidime (taz, 10 mg/kg/d), tPA (2-20 mg/kg/d), SK (4,000-100,000 U/kg/d) were given i.p. twice daily on days 2-6.
RESULTS: The mean survival on day 7 for n=4 replicate experiments (32-48 mice/tx) was: unburned (100%), burned/no infection (100%), B/I: saline treated (0%), SK (<5% at all dose levels), tPA (<5% at all dose levels), Taz (19.8%), Taz+tPA (<25% at all dose levels, p=NS vs Taz alone), Taz +SK 4,000 U/kg/d (46.5%, p<0.05 vs Taz alone). Higher dosages of SK (40,000-200,000 U/kg/d) resulted in a trend toward decreased survival. Consistent with improved survival with "low-dose" SK +Taz, parallel experiments demonstrated significantly (P<0.05) lower TNF-a, higher IL-10 levels and fewer organisms (liver) than all other regimens.
CONCLUSIONS: The addition of SK, a systemic fibrinolytic, significantly improved survival compared to antibiotics alone in experimental sepsis. The survival benefit was inversely related to dose. The highly fibrin-specific tPA had no effect on survival.

120. Multi-center evaluation of community acquired pneumonia: patterns of guideline adherence over two pneumonia seasons. *Thomas A. Wolfe, Pharm.D.,* Bonnie DeLor, Pharm.D., BCPS, Lisa Greenstein, Pharm.D., Great Lakes Pneumonia Outcomes Evaluation Team; Pfizer, Inc., Columbus, OH; Pfizer, Inc., Detroit, MI; Pfizer, Inc., Cincinnati, OH.

PURPOSE: This multi-center study evaluated the management of hospitalized patients with community-acquired pneumonia (CAP) over a two-year period to compare CAP management strategies to established guidelines (Joint Commission Core Measures [JCAHO-CM] and Infectious Disease Society of America [IDSA]).
METHODS: Medical records were reviewed from patients admitted with a diagnosis of CAP at Midwestern hospitals between October 1 and April 30, 2000-2001(Phase I) and 2001-2002 (Phase II). 840 in Phase I (20 hospitals) and 581 in Phase II (13 hospitals) patients were identified.
RESULTS: The most common initial empiric antibiotic regimens were Levofloxacin (27.3% and 30.5%) and 3rd generation Cephalosporin plus azithromycin (23.7% and 34.4%) for Phase I and Phase II, respectively. Antibiotic regimens in Phase II were more likely to be consistent with IDSA recommendations for "General Medical Ward" than Phase I (76.7 vs 62%, p<0.001), but not different in ICU patients (36.4 vs 51.2%, p>0.05). Similar JCAHO-CM were compared: oxygenation assessment within 24 hours (96.9 vs 97.3%, p>0.05), pneumococcal vaccination status (23.2 vs 26.1%, p>0.05), blood cultures prior to antibiotics (79 vs 77%, p>0.05), smoking cessation counseling (22.2 vs 22%, p>0.05), and antibiotic administration within 8 hours of admission (89.9 vs 87%, p>0.05). The average time to first antibiotic dose was 4.2 and 4.5 hours (95% CI, -0.81-0.17, p>0.5).
CONCLUSIONS: Appropriate antibiotic utilization according to IDSA guidelines did increase over time in the most common group of CAP patients. However, adherence to other management recommendations changed very little. Efforts to educate providers on appropriate management beyond antibiotic selection are warranted.

121E. Comparison of microarray data between two quinolone-resistant *Streptococcus pneumoniae* isolates. *Holly L. Hoffman, Pharm.D.,* Isaac F. Mitropoulos, Pharm.D. candidate, Carsten Rosenow, Ph.D., W. Michael McShan, Ph.D.; University of Oklahoma, Oklahoma City, OK; Affymetrix, Santa Clara, CA.

Presented at the 103rd General Meeting of the American Society of Microbiology, Washington, DC, May 22, 2003.

122. Comparative pharmacodynamic profiles of ciprofloxacin and levofloxacin against *P. aeruginosa*: impact of increasing resistance. *Roger L. White, Pharm.D.,* John A. Bosso, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: AUC/MIC and C_{max}/MIC are associated with efficacy of ciprofloxacin© and levofloxacin (L). Increases in resistance necessitate periodic reevaluation of these parameters.
METHODS: Using a database of MIC studies, we assessed trends in MIC_{90}s of C and L using North American studies published from 1992-2000. Weighted (based on number of isolates) geometric mean (WGM) MIC_{90}s were calculated. Trends were assessed by linear regression of log WGM values. Literature pharmacokinetic (PK) values were used to simulate steady-state

unbound serum concentration-time profiles (70kg adult) for IV doses of C 400 mg q8 -12h and L 500–750 mg q24h. Simulations were performed at creatinine clearances (CrCl) of 100, 75, 50, and 25 ml/minute using published CrCl/drug clearance relationships and dosing was adjusted for renal dysfunction. Using WGM MIC_{90}s from 2002, $AUC_{0\text{-}24\ hrs}/MIC_{90}$ and Cmax/ MIC_{90} were calculated and considered acceptable for monotherapy if ≥125 and ≥8, respectively.
RESULTS: WGM MIC_{90}s ranged from 1.4 (1992) to 16 µg/ml (2002) for C and 2.0 (1992) to 32 µg/ml (2002) for L. The increases in MICs were consistent, with maximum fold changes between any sequential years of 2.2 and 2.8 for C and L, respectively. Irrespective of drug, regimen, or CrCl, no pharmacodynamic (PD) parameters were acceptable. Over the range of CrCl studied, $AUC_{0\text{-}24\ hrs}/MIC_{90}$ for the lower dosage regimens were: 1.1-1.7 for C and 1.1-1.9 for L; Cmax/ MIC_{90} 0.13-0.14 for C and 0.10-0.16 for L. PD parameters for the higher dosage regimens were: $AUC_{0\text{-}24\ hrs}/MIC_{90}$ 1.5-2.6 for C and 1.6-2.8 for L; Cmax/ MIC_{90} 0.14-0.17 for C and 0.19-0.23 for L.
CONCLUSIONS: Over this 11 year period, large increases in MIC_{90}s against *P. aeruginosa* were found. Although C is more potent, the more favorable PK profile of L results in similar PD profiles for both agents. Based on these profiles, no differences in efficacy against *P. aeruginosa* would be expected. However, these findings should be verified by comparative clinical trials.

123. Outcomes and risk factors in patients with ceftazidime non-susceptible *Enterobacter cloacae* bacteremia. *Menglin L. Lin, Pharm.D.,* Katie J. Suda, Pharm.D., Angela B. Link; Pharm.D., Bryan L. Love, Pharm.D., BCPS; Baptist Memorial Health Care, Memphis, TN.

PURPOSE: *Enterobacter cloacae* (EC) is an emerging nosocomial pathogen associated with significant morbidity and mortality. At Baptist Memorial Hospital, Memphis, the number of EC isolates has doubled with a decrease in anti-infective susceptibility. The purpose of this study was to investigate patient outcomes and determine risk factors (RF) for acquisition of ceftazidime non-susceptible (CR) EC bacteremia.
METHODS: A retrospective study reviewed 27 patients with EC bacteremia as identified by microbiology reports from 8/2001-8/2002. Data collected included culture and sensitivity information, antibiotics received, and patient demographics and outcomes. Patients were stratified into two groups based on ceftazidime susceptibility. Statistical analysis was performed using Student t-test and Fischer's Exact Test. A p value ≤0.05 was considered significant.
RESULTS: Twenty-nine non-duplicate isolates were obtained (64±15 years; 55% male), 59% were ceftazidime susceptible (CS). Non-significant RF for CR included ICU admission on culture date (OR=5.4), hemodialysis (OR=2), and catheter as the infection source (OR=1.5). Negative non-significant RF included pulmonary concomitant infection (OR=0.2), urine (OR=0.3) and lungs (OR=0.4) as the infection source. Interestingly, CR received vancomycin more frequently prior to obtaining the culture (p=0.003) and CS received levofloxacin more frequently after culture obtained (p=0.01). Patient demographics, length of stay, APACHEII and mortality were not significantly different between groups.
CONCLUSIONS: This study was not able to establish significant RF for CR EC bacteremia. Although not statistically significant, patients cultured in the ICU and receiving hemodialysis were more likely to have CR isolates. Patients with lung and urine as the infection source and concomitant pulmonary infection were less likely to have CR isolates.

124E. Genome-wide expression profile analysis reveals genes coordinately regulated with MDR1 in association with the acquisition of fluconazole resistance in clinical isolates of *Candida albicans*. *P. David Rogers, Pharm.D., Ph.D.,* Katherine S. Barker, Ph.D., Joachim Morschhäuser, Ph.D.; University of Tennessee Health Sciences Center, Memphis, TN; University of Wurzburg, Wurzburg, Germany.

Presented at the 15th Congress of the International Society for Human and Animal Mycology, San Antonio, TX, May 25-29, 2003.

125E. Genome-wide expression profiling of experimentally induced amphotericin B resistance in *Candida albicans*. P. David Rogers, Pharm.D., Ph.D., *Sarah Crisp,* Katherine S. Barker, Ph.D., Nathan Wiederhold, Pharm.D., Russell E. Lewis, Pharm.D.; University of Tennessee Health Science Center, Memphis, TN.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

126. Proteomic analysis of azole antifungal resistance in *Candida albicans* by 2D-SDS-PAGE and peptide mass fingerprinting. Massoumeh Z. Hooshdaran, Ph.D., George M. Hilliard, Ph.D., Katherine S. Barker, Ph.D., Joachim Morschhauser, Ph.D., *P. David Rogers, Pharm.D., Ph.D.*; University of Tennessee Health Sciences Center, Memphis, TN; University of Wurzburg, Wurzburg, Germany.

PURPOSE: The efflux pumps Cdr1p, Cdr2p and Mdr1p, as well as the target of the azoles, lanosterol demethylase (Erg11p), have been implicated in azole resistance. The aim of the present study was to identify proteins that are differentially expressed in, and hence associated with, azole antifungal resistance in *C. albicans*.
METHODS: Two isogenic, matched, clinical isolates of *C. albicans* were obtained from an AIDS patient with oropharyngeal candidiasis who failed fluconazole therapy (isolates 2-79; MIC=0.25 µg/ml and 12-99; MIC>64 µg/ml). The isolates were grown to early exponential phase and the protein fraction was precipitated, subjected to 2-D-SDS-PAGE, and stained with Coomassie blue. Gel images were analyzed with PDQuest software. Experiments were performed independently in triplicate. Protein spots were identified by MALDI-TOF-TOF MS peptide mass fingerprinting using a *C. albicans* ORF database formatted for PROWL software.
RESULTS: A total of 24 protein spots were observed to be differentially expressed in these isolates, 21 of which were positively identified. Proteins differentially expressed in association with resistance included those encoded by genes we have previously shown to be differentially expressed in these isolates (Grp2p, Ifd1p, Ifd4p, Ifd5p), proteins involved in the ergosterol biosynthesis pathway (Erg10p, Erg13p), and proteins newly associated with this phenotype (Ilv5p, Ifd6p, Lys21p, Gpm1p).
CONCLUSIONS: This is the first report of genome-wide peptide mass fingerprinting for the identification of proteins associated with azole resistance in *C. albicans*. These results are consistent with previous findings from gene expression profiling studies and implicate additional proteins that are differentially expressed in association with azole resistance independent of transcriptional regulation.

127E. Gene expression and proteomic profile analysis reveals novel gene and protein expression patterns associated with fluconazole resistance in clinical isolates of *Candida albicans*. *P. David Rogers, Pharm.D., Ph.D.,* Katherine S. Barker, Ph.D., Ziba Hooshdaran, Ph.D., George M. Hilliard, Ph.D., Edwin Cummings, B.S., Janet Brown, B.S., Joachim Morschhauser, Ph.D.; University of Tennessee Health Sciences Center, Memphis, TN; University of Wurzburg, Wurzburg, Germany.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

128. In vitro killing of ertapenem compared to several other antimicrobials against extended-spectrum β-lactamase *K. pneumoniae*. *David S. Burgess, Pharm.D.,* Ronald G. Hall, II, Pharm.D.; University of Texas, Austin, TX; University of Texas Health Science Center, San Antonio, TX; Texas Tech University Health Science Center, Dallas, TX; North Texas Veterans Healthcare System, Dallas, TX.

PURPOSE: Extended-spectrum β-lactamase (ESBL) producing organisms are a growing problem. Currently, carbapenems are considered the drug of choice for treating these serious infections. Ertapenem is a new carbapenem with a pharmacokinetic profile compatible with a once-a-day dosing regimen. The purpose of this study was to evaluate the in vitro killing of ertapenem compared to several other antimicrobials against ESBL producing *K. pneumoniae*.
METHODS: MICs were performed against 8 clinical isolates of ESBL producing *K. pneumoniae* using NCCLS guidelines for the following antimicrobials: ertapenem, imipenem, ceftriaxone, cefepime, piperacillin/tazobactam, levofloxacin, and tobramycin. Three isolates produced SHV enzymes (SHV-2, -5, and -18) and five isolates produced TEM enzymes (TEM-3, -5, -10, -12, and -26). Time-kill studies were performed for a standard inoculum with the following drug concentrations (µg/ml): ertapenem (1.5), imipenem (4), ceftriaxone (1.5), cefepime (20), piperacillin/tazobactam (40/5), levofloxacin (4), and tobramycin (4). Samples were taken at 0, 2, 4, 6, 8, 12, and 24 hours then serially diluted if necessary and plated on TSA plates. After incubation for 24 hours at 35C, colony counts were determined using a laser colony counter.
RESULTS: MICs (µg/ml) were: ertapenem (0.125-2), imipenem (0.5-2), ceftriaxone (0.5-256), cefepime (8-64), piperacillin/tazobactam (16/4->1024/4), levofloxacin (1-8), and tobramycin (8-64). Only imipenem and levofloxacin reached and maintained bactericidal (≥ 3 log killing) activity over the entire 24 hours for all isolates followed closely by ertapenem (7 isolates), and cefepime (6 isolates). Piperacillin/tazobactam maintained bactericidal activity against 2 isolates. Ceftriaxone and tobramycin did not reach bactericidal activity against any of the isolates.
CONCLUSIONS: Ertapenem displays similar in vitro killing to other carbapenems against ESBL *K. pneumoniae*. In addition, levofloxacin and cefepime displayed significantly better killing than piperacillin/tazobactam, ceftriaxone, and tobramycin against these isolates of ESBL *K. pneumoniae*. The clinical significance of these results warrants further investigation.

129. Evaluation of current NCCLS breakpoints for extended-spectrum cephalosporins against Gram-negative bacteria based on pharmacodynamic principles. *David S. Burgess, Pharm.D.,* Ronald G. Hall, II, Pharm.D.; University of Texas, Austin, TX; University of Texas Health Science Center, San Antonio, TX; Texas Tech University Health Science Center, Dallas, TX; North Texas Veterans Healthcare System, Dallas, TX.

PURPOSE: For β-lactams, time above the MIC is the major pharmacodynamic parameter that predicts outcomes. The purpose of this study was to evaluate the current NCCLS breakpoints for the extended spectrum cephalosporins based on pharmacodynamics and recommend new

breakpoints if needed for each cephalosporin evaluated based on maximizing the pharmacodynamics.
METHODS: The following antimicrobial regimens were evaluated for a 70 kg patient: ceftriaxone 1 g and 2 g q24h, ceftazidime 1 g and 2 g q8h, cefepime 1 g and 2 g q12h, and cefepime 1 g and 2 g q8h. The volume of distribution, half-life, and protein binding obtained from peer-reviewed published literature and used for each antimicrobial was: ceftriaxone (0.11 ± 0.02 L/kg, 7.65 ± 1.30 hours, 95%), ceftazidime (0.21 ± 0.03 L/kg, 1.95 ± 0.25 hours, 17%), cefepime (0.26 ± 0.04 L/kg, 2.23 ± 0.35 hours, 20%). The % T>MIC was determined for 10,000 simulated patients using Crystal Ball (Decisioneering, Inc., Denver, CO) for a MIC range from 0.5-64 µg/ml. The probabilities of obtaining free T>MIC 20-100% of the dosing interval was determined for each MIC. A probability of 95% target attainment was defined as optimal T>MIC.
RESULTS: The probability of obtaining T>MIC of 50-60% at the current breakpoint for each antimicrobial was: 10-24% for ceftriaxone 1 g QD, 65-81% for ceftriaxone 2g QD, 76-96% for ceftazidime 1 g q8h, 99-100% for ceftazidime 2 g q8h, 2-23% for cefepime 1 g q12h, 61-90% for cefepime 2 g q12h, 77-94% for cefepime 1 g q8h, and 99-100% for cefepime 2 g q8h. The highest MIC at which the probability was ≥ 95%for the T>MIC of 50-60% of the dosing interval for each antimicrobial was: ceftriaxone (1-2 µg/ml), ceftazidime (4-8 µg/ml), cefepime q12h dosing (2-4 µg/ml), and cefepime q8h dosing (4-8 µg/ml).
CONCLUSIONS: The current breakpoints for each extended spectrum cephalosporin do not allow for optimal %T>MIC. Based on maximizing the pharmacodynamic parameter, the proposed breakpoints for susceptible, intermediate, and resistance would be 1, 2, and 4 µg/ml for ceftriaxone; 4, 8,and 16 µg/ml for ceftazidime; 2, 4, and 8 µg/ml for cefepime when dosed q12h; and 4, 8, and 16 µg/ml for cefepime when dosed q8h.

130E. Influence of linezolid and vancomycin on the release of α-hemolysin from methicillin resistant *Staphylococcus aureus*. *Elizabeth A. Coyle, Pharm.D.,* Russell E. Lewis, Pharm.D., Kenneth V. I. Rolston, M.D., Randall A. Prince, Pharm.D.; University of Houston, Houston, TX.

Presented at the 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

131. Pharmacodynamics of continuous infusion cefepime and piperacillin-tazobactam against extended spectrum β-lactamase producing organisms using Monte Carlo simulation. *Christopher R. Frei, Pharm.D., M.S.,* Alicia M. Reese, Pharm.D., BCPS, David S. Burgess, Pharm.D.; University of Texas; University of Texas Health Science Center, San Antonio, TX.

BACKGROUND: Bacteria that produce extended spectrum β-lactamase (ESBLs) are an emerging problem in infectious disease. Since time above the MIC is the parameter that best correlates with *in vivo* activity, it has been suggested that β-lactams should be administered by continuous infusion (CI) to maximize time above MIC.
PURPOSE: This study evaluates the pharmacodynamics of CI cefepime and piperacillin-tazobactam against ESBLs by employing a computer modeling technique known as Monte Carlo simulation.
METHODS: In accordance with NCCLS guidelines, MICs were determined in triplicate for cefepime and piperacillin-tazobactam among 39, non-duplicate, ESBL-producing isolates, from University Hospital. ESBL strips of ceftazidime with and without clavulanic acid were used for ESBL confirmation. Our research group previously determined the pharmacokinetic parameters of CI cefepime (3g and 4g) and CI piperacillin-tazobactam (6.75 g and 13.5 g) in normal healthy volunteers (Clin Ther 2002;24:1090-1104, Clin Ther 2000;22:66-75). Pharmacokinetic and MIC data were integrated using Crystal Ball (Decisioneering, Inc., Denver, CO) to determine the probability of achieving 1, 2, or 4 times Css/MIC for 10,000 simulated subjects.
RESULTS: The MIC_{50}, MIC_{90}, and %S for cefepime and piperacillin-tazobactam were 8 µg/ml, 16 µg/ml, and 0% and 64/4 µg/ml, 1024/4 µg/ml, and 33%, respectively. All isolates were reported to be resistant to cefepime as recommended by NCCLS; however, if a break point of 8 µg/ml were used, then the % S to cefepime would be 31%. The median Css/MIC was as follows: cefepime 3 g CI (1.9), cefepime 4 g CI (2.7), piperacillin-tazobactam 6.75 g (0.2), and piperacillin-tazobactam 13.5 g (0.6). The probability of obtaining a target of 1, 2, and 4 times Css/MIC were as follows: cefepime 3 g CI (83%, 46%, 25%), cefepime 4 g CI (94%, 77%, 31%), piperacillin-tazobactam 6.75 g CI (26%, 10%, 0%), and piperacillin-tazobactam 13.5 g CI (44%, 31%, 17%).
CONCLUSIONS: Examination of MICs indicates a high level of resistance to both cefepime and piperacillin-tazobactam among ESBLs. These data suggest that the probability of obtaining a target Css/MIC is greater with continuous infusion cefepime than with piperacillin-tazobactam; however, neither antimicrobial consistently attained adequate Css/MIC for the treatment of ESBL infections.

132E. In vitro pharmacodynamics of rapid vs continuous infusion amphotericin B deoxycholate in the presence of human serum albumin. *Nathan P. Wiederhold, Pharm.D.,* Dimitrios P. Kontoyiannis, M.D. Sc.D., Russell E. Lewis, Pharm.D.; University of Houston; University of Texas M.D. Anderson Cancer Center, Houston, TX.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

133E. Antibacterial activity of linezolid and vancomycin in an in vitro pharmacodynamic model of Gram-positive catheter-related bloodstream infection. *Nathan P. Wiederhold, Pharm.D.,* Elizabeth A. Coyle, Pharm.D., Jingduan Chi, Ph.D., Issam I. Raad, M.D., Randall A. Prince, Pharm.D., Russell E. Lewis, Pharm.D.; University of Houston; University of Texas M.D. Anderson Cancer Center, Houston, TX.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

134E. In vivo pharmacodynamics of caspofungin in a murine model of invasive pulmonary aspergillosis. *Nathan P. Wiederhold, Pharm.D.,* Dimitrios P. Kontoyiannis, M.D., Sc.D., Jingduan Chi, Ph.D., Randall A. Prince, Pharm. D., Vincent H. Tam, Pharm.D., Russell E. Lewis, Pharm.D.; University of Houston; University of Texas M.D. Anderson Cancer Center, Houston, TX.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

135. Antibiotic use and emergence of methicillin-resistant *Staphylococcus aureus* over an 8-year period: an analysis of 12 different time periods. *John F. Mohr, Pharm.D.,* Luis Ostrosky-Zeichner, M.D., Audrey Wanger, Ph.D., Charles D. Ericsson, M.D.; University of Texas Health Science Center, Houston, TX.

PURPOSE: The purpose of this study was to evaluate relationships between all antibiotic use and the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) during multiple time periods within an 8-year period.
METHODS: MRSA rate and antibiotic utilization was collected from 1995 to 2002 for a 700-bed, private, university affiliated hospital located in the Texas Medical Center. Susceptibility data was expressed as percent of isolates resistant to methicillin and antibiotic utilization was expressed as Daily Doses Dispensed/1000 patient days. Multiple linear regression analysis was performed against the rate of MRSA and various antibiotic use for 12 different time periods within the 8 year study period.
RESULTS: 23 antibiotics and 6 classes were evaluated for their association with MRSA emergence over the 12 time periods. There were 58/339 possible statistically significant relationships ($p<0.05$) identified. There were 28/58 relationships between increasing antibiotic use and increasing MRSA and 30/58 relationships between decreasing antibiotic use and increasing MRSA. For 7/12 (58%) time periods, including the 8-year period, increasing total fluoroquinolone use was related to increasing MRSA. 5/12 (42%) time periods, increasing vancomycin use was related to increasing MRSA. Decreasing third generation cephalosporin use was related to increasing MRSA in 4/12 (33%) of the periods. There were 7, 3 and 8 antibiotics with 3/12, 2/12 and 1/12 relationships, respectively. Total fluoroquinolone use had a relationship in each of the time periods evaluated.
CONCLUSIONS: When evaluating the relationships between antibiotic use and prevalence of MRSA, it is important to consider different time periods. Total fluoroquinolone use had relationships in every time period studied. The greatest number of relationships between antibiotic use and emergence of MRSA was seen when analyzing the total 8 year period. Analyses across shorter time periods risked failing to detect associations.

136. Pharmacodynamics of intermittent piperacillin/tazobactam and cefepime against extended-spectrum β-lactamase producing organisms using Monte Carlo simulation. *Alicia M. Reese, Pharm.D., BCPS,* Christopher R. Frei, Pharm.D., M.S., David S. Burgess, Pharm.D.; University of Texas at Austin, Austin, TX; University of Texas Health Science Center, San Antonio, TX.

BACKGROUND: Treatment of infectious diseases is becoming more difficult due to the increasing incidence of extended-spectrum β-lactamase (ESBL) producing organisms. For β-lactams, clinical outcomes have are related to the proportion of the dosing interval that the drug concentrations remain above a pathogen's MIC (%T>MIC). The use of piperacillin/tazobactam and cefepime to treat infections with ESBL-producing gram-negative organisms is controversial.
PURPOSE: This study used Monte Carlo simulation to compare the pharmacodynamics of intermittent piperacillin/tazobactam and cefepime against ESBL-producing organisms from a tertiary care medical center.
METHODS: MIC's were determined in triplicate using broth microdilution according to NCCLS guidelines for 39 non-duplicate clinical ESBL-producing isolates from University Hospital. ESBL E-strips with ceftazidime ± clavulanate were used for confirmation of ESBL production. Pharmacokinetic and protein binding data for piperacillin/tazobactam and cefepime were collected from peer-reviewed studies of normal healthy volunteers. Monte Carlo analysis was performed for 10,000 simulated subjects using Crystal Ball (Decisioneering, Inc., Denver, Colorado) for piperacillin/tazobactam 3.375g q6h and q4h and 4.5g q8h and cefepime 1g q8h and 1g and 2g q12h. The probabilities of obtaining free %T>MIC of 20-100% were determined.
RESULTS: MIC50, MIC90, and %S were 64/4, 1024/4, and 33% for

piperacillin/tazobactam and 8, 16, and 0% for cefepime, respectively. All isolates were reported resistant to cefepime as recommended by NCCLS; if the 8 µg/ml breakpoint were used, 31% would have been susceptible. For piperacillin/tazobactam, the median %T>MIC ranged from 16% for 3.375g q6h and 4.5g q8h to 26% for 3.375g q4h; and the target attainment rates for 40% T>MIC were 43%, 27%, and 17% for 3.375 g q4h and q6h and 4.5g q8h, respectively. For cefepime, the median %T>MIC ranged from 44% for 1g q12h to 69% for 1g q8h; and target attainment rates for 50% T>MIC were 37% for 1g q12h, 76-78% for 1g q8h and 2g q12h.
CONCLUSIONS: These ESBL-producing organisms, according to their MIC's, showed considerable resistance to piperacillin/tazobactam and cefepime. Overall, the target attainment rates for cefepime were higher than those for piperacillin/tazobactam; however, neither agent provided adequate target attainment rates for the treatment of infection with these ESBL organisms.

Medication Safety

137. Medication therapy review of newly admitted patients. *Ann Kathryn Rhodes, Pharm.D.,* Jon Kennedy, Pharm.D., Lynn Chestnutt, R.Ph., Lih-Jen Wang, Pharm.D.; Columbus Regional Medical Center, Columbus, GA.

BACKGROUND: Medical errors are the eighth leading cause of death in the United States. The pharmacist-conducted medication history is a traditional, yet overlooked clinical service. A vital component of quality care and medication error prevention is pharmacist conducted medication histories. Medication therapy review of newly admitted patients (MRNA) involves the evaluation of medication-related discrepancies identified upon admission through a pharmacist-conducted medication history program.
PURPOSE: To implement and evaluate the effects of a MRNA on quality of care upon hospital admission, risk of drug misadventure, and patient outcomes.
METHODS: Within 24 hours from the time on the nurses' census records, patients were selected. The pharmacist or directly supervised intern would take a medication history from the patient. After collection of medication-related data, opportunities for intervention were identified. Interventions were documented using specific categories in both the pharmacy computer system and a spreadsheet. The types of medication-related problems were categorized and tracked to identify areas for pharmacists' intervention. An impact factor was retrospectively applied to each intervention.
RESULTS: There were 82 interventions out of 172 medication reviews completed over a five-month period from August 2002 to January 2003. The most frequent interventions were patient education, order clarification and dose adjustments. The most clinically significant interventions were changing dosages, clarifying home medications, clarifying orders, stopping/holding a drug, and discontinuation of a medication.

138. Improving medication safety through the reduction of polypharmacy in a large capitated population. *Barbara J. Zarowitz, Pharm.D., FCCP, BCPS,* Lesia Stebelsky, B.Sc.Phm., Fadwa Gillanders, Pharm.D., Tanya Romain, Pharm.D., Carol Reneski, B.S., Roger Austin, M.S., the PRIM Safety Investigators; Henry Ford Health System, Detroit, MI.

PURPOSE: The goals of this program are to improve medication safety and lower drug cost by reducing the overuse, underuse, and misuse of medications (polypharmacy).
METHODS: Six months of pharmacy claims data for 214,364 capitated patients were queried using graphics query language to identify those at risk of harm from polypharmacy. High-risk patients were defined as those receiving sildenafil plus a nitrate A), ≥ 2 benzodiazepines B), ≥ 2 narcotic analgesics C), ≥ 3 oral antidiabetic agents D), or ≥ 5 medications E) concurrently for >119 days, in a 6 month period. Patient-specific reports outlining medications, dose, fill frequency, and days of therapy, were provided to primary care physicians with review and follow-up by a pharmacist. Interventions were designed to reduce rates/1,000 of A, B, C, and D by 89%, 20%, 20%, and 20%, respectively. Six months following intervention, the cohort queries were repeated.
RESULTS: Two percent (2,037/214,364) of patients met one or more polypharmacy criteria. Post intervention rates/1,000 were reduced for A (0.4 to 0.01/1,000 [97.5%]), B (5 to 1.3/1,000 [74%]), C (18.3 to 3.1/1,000 [83%]), D (2.3 to 0.6/1,000 [74%]), and E (8.5 to 4.6/1,000 [46%]), respectively. Mean utilization decreased from 4.6 to 2.2 prescriptions (RxPMPM) (51.5%) and mean drug cost ($PMPM) decreased from $222 to $113 (48.8%), per member per month. Drug use without indication (9%), non-adherence (11%), lower cost alternative (11%), and untreated indication (19%) were the most common correctable findings.
CONCLUSIONS: Drug cost and utilization in high-risk polypharmacy situations was reduced. Future studies will quantify cost avoided by preventing harm.

139. The evaluation of new terminology for classifying the severity of ambulatory medical errors. *Holly E. Rogers, Pharm.D., C.* Andrew Brown, M.D., M.P.H., Amy C. Alvarez, M.A., Lisa M. Murphey, Pharm.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: An on-line mechanism for reporting medical errors, including a severity scale for classifying the errors, was recently instituted at a university medical center. However, the reporting mechanism was primarily designed for the inpatient arena, and the severity scale in its original terminology was not applicable to the ambulatory setting. Therefore, a new scale with terminology specifically tailored to the ambulatory setting was developed. The purpose of this project was to test the ambulatory severity scale for correlation to the original scale, applicability to the ambulatory area, and user satisfaction.
METHODS: Physicians, nurses and pharmacists were selected as participants. Each group was administered a survey consisting of 10 ambulatory patient scenarios. They were to indicate which severity classification each scenario best fit from the original scale and the new scale, rate their satisfaction with the new scale, and rate the applicability of the new scale to the ambulatory setting.
RESULTS: The classification of each scenario's severity was consistent with less than 1 severity point difference among the response averages. Although in general, nurses and pharmacists tended to classify the severity of an error with at a lower score than physicians. The overall satisfaction score was 2 = satisfied; however, the overall applicability score could not be determined.
CONCLUSIONS: The severity scale developed for use in the ambulatory setting correlates closely with the original scale developed for inpatient care and the medical personnel's overall satisfaction with the new terminology should help facilitate medical error reporting in this setting.

140. The role of medications as determinant of falls in the hospitalized inpatient. *John A Noviasky, R.Ph., Pharm.D.,* Kathryn Ward, R.N., Nancy Traxel, B.S., R.N.; St. Elizabeth Medical Center, Utica, NY.

PURPOSE: To determine the role of medications and other variables associated with falls in the acute care hospitalized patient.
METHODS: Patients who had fallen during time period of study (July to December 2002) were identified and medication information (by class and by number of classes of medication), as well as patient and environmental variables were collected.
RESULTS: Ninety-seven patients were identified as having fallen during period of study and medication presence is as follows; Antihypertensive (56.7%), Antianxiety/Sedative/Hypnotics (55.7%), Antipsychotic/Alzheimers (37%), Antidepressant (35.1%), Analgesics/narcotics/muscle relaxants (35.1%), Anticonvulsants (32.0%), Laxative/diuretic (29.9%), Antihistamine (23.7%), Hypoglycemics (21.6%), Antiparkinson (9.3%), Bi-polar medications (3.1%) and Barbiturates (0%). There also appeared to be relationship between number of medication classes and falls (%); 0 (8.2%), 1 (10.3%), 2 (18.6%), 3 (20.6%), 4 (13.4%), 5 (16.5%), ≥ 6 (12.4%). Almost half of all falls (46.3%) were reported in those ≥ 70 years old. Other patient variables which appeared to influence falls were length of stay >3days (71.1%), confusion before fall (68.0%), assistance with waste elimination necessary (34.0%), and history of fall within 6 months (26.8%). Certain variables such as day of week, primary language, use of bed alarm and use of restraints did not seem to influence occurrence of falls in this population.
CONCLUSIONS: While medications play an important part in patient falls as almost all patients were on at least one class of drugs targeted (91.8%), other easily identifiable variables should be considered in development of fall-risk assessment tool.

Nephrology

141E. Lanthanum carbonate (Fosrenol™) causes significant reductions in serum phosphorus and calcium X phosphorus product in a dose-ranging, placebo-controlled study. William F. Finn, M.D., Melanie S. Joy, M.D., *Chris Paap, Pharm.D., FCCP, BCPS*; University of North Carolina, Chapel Hill, NC; Shire US Inc., Newport, KY.

Presented at the 40th ERA-EDTA World Congress of Nephrology, Berlin, Germany, June 8-12, 2003.

142E. The pharmacology of a new phosphate binder, lanthanum carbonate (Fosrenol™). Stephen J.P. Damment, Ph.D., Wilson Totten, *Sherry L. Andes, Pharm.D., B.S.Pharm.*; Shire Pharmaceutical Development, Ltd., Basingstoke, UK; Shire US Inc., Newport, KY.

Presented at the 40th ERA-EDTA World Congress of Nephrology, Berlin, Germany, 8-12 June, 2003.

143E. The novel, non-aluminum, non-calcium phosphate binder, lanthanum carbonate (Fosrenol™), is an effective treatment for hyperphosphatemia and has a good safety profile. Alastair J. Hutchison, M.D., *Sherry L. Andes, Pharm.D.*; Manchester Royal Infirmary, Manchester, United Kingdom; Shire US Inc., Newport, KY.

Presented at the Annual Meeting of the American Society of Nephrology, Philadelphia, PA, November 1-4, 2002.

144. Evaluation of OAT activity in a human-derived renal proximal tubule (HK-2) cell line. Minori Kinjo, B.S., Tahira Iqbal, Ph.D., *Thomas C. Dowling, Pharm.D., Ph.D.*; University of Maryland, Baltimore, MD.

PURPOSE: The kidney plays a primary role in elimination of numerous drugs, toxins and metabolites. The purpose of this study was to evaluate organic anion transport (OAT) activity, using para-aminohippurate (PAH), in a new human kidney proximal tubule (HK-2) cell line.
METHODS: HK-2 cells were grown in supplemented RPMI media, and seeded onto collagen-coated membrane inserts at a density of $5.0x10^5$ cells/ml. Monolayer integrity was assessed by ^{14}C-Mannitol transport and transepithelial electrical resistance (TEER) measurements. Cell viability was assessed using trypan blue exclusion at PAH concentrations of 4.62 µmol-9.25mM. Transepithelial transport was studied in the basolateral-to-apical (B/A) and apical-to-basolateral (A/B) directions. Cells were incubated with the OAT inhibitors probenecid (200 µmol) and acetyl-PAH (5.8nM), a metabolite of PAH, for 60 minutes prior to co-incubation with PAH (92.5 µmol). PAH concentrations were determined using HPLC/UV.
RESULTS: HK-2 cell viability was 99.3±0.35% at the concentrations tested. The apparent permeability of ^{14}C-mannitol ranged from 1.12 to $11.7x10^{-4}$ cm^2/sec. TEER values ranged from 56.43 to 77.55 cm^2/sec. The Papp values for PAH were $3.98x10^{-8}$ and $3.59x10^{-9}$ cm^2/sec for B/A and A/B transport, respectively. PAH transport (B/A) rates ranged from 0.15 to 10.01 µmol /minute and transport was linear across the concentration range tested. Transport inhibition was achieved with probenecid (17.8 ± 1.8%) and aPAH (30.0 ± 1.1%), suggesting that aPAH is a more potent inhibitor of OAT activity than probenecid.
CONCLUSIONS: These results indicate that anionic transport can be assessed using HK-2 cells. Further development of the OAT transport model is needed to evaluate its use as a surrogate for in vivo studies.

145E. Lanthanum carbonate (Fosrenol™) does not affect the pharmacokinetics of warfarin. Garrick Fiddler, M.D., *David A. Mays, Pharm.D., MBA, BCPS*; Shire Pharmaceutical Development Ltd., Basingstoke, United Kingdom; Shire Pharmaceutical Development Inc., Rockville, MD.

Presented at the Clinical Meeting of the National Kidney Foundation, Dallas, TX, April 2-6, 2003.

146E. Lanthanum carbonate (Fosrenol™) does not affect the pharmacokinetics of concomitant treatment with digoxin. Garrick Fiddler, M.D., Jorg Taubel, M.D., *David A. Mays, Pharm.D., MBA, BCPS*; Shire Pharmaceutical Development, Ltd., Basingstoke, United Kingdom; Royal Masonic Hospital, London, United Kingdom; Shire Pharmaceutical Development, Inc., Rockville, MD.

Presented at the Clinical Meeting of the National Kidney Foundation, Dallas, TX, April 2-6, 2003.

147E. No pharmacokinetic interaction between lanthanum carbonate (Fosrenol™) and metoprolol. Garrick Fiddler, M.D., Jorg Taubel, M.D., *David A. Mays, Pharm.D., MBA, BCPS*; Shire Pharmaceutical Development, Ltd., Basingstoke, United Kingdom; Royal Masonic Hospital, London, United Kingdom; Shire Pharmaceutical Development, Inc., Rockville, MD.

Presented at the Clinical Meeting of the National Kidney Foundation, Dallas, TX, April 2-6, 2003.

148E. Pharmacokinetics of oral linezolid inpatients on peritoneal dialysis. *Suzette R. Gendjar, Pharm.D.,* Brad Moriyama, Pharm.D., Mark D. Faber, M.D., Diane Borg, R.N., Dave Edwards, Ph.D., *Elaine M. Bailey, Pharm.D.*; Henry Ford Hospital, Detroit, MI; National Institutes of Health, Bethesda, MD; Wayne State University, Detroit, MI; Ortho-McNeil Pharmaceutical, Harrison Township, MI.

Presented at the 2001 World Congress of Nephrology of the American Society of Nephrology, San Francisco, CA, September 23-29, 2003.

149E. Chronic kidney disease management in an ambulatory care practice network: assessment for a renal monitoring service in community health clinics. *Harita R. Patel, Pharm.D.,* Maria C. Pruchnicki, Pharm.D., BCPS, Laura E. Hall, Pharm.D., BCPS; Ohio State University, Columbus, OH.

Presented at the Annual Research Forum of the Ohio Pharmacists Association, Columbus, OH, April 11, 2003.

150E. A comparison of Intravenous and oral iron therapy in children receiving hemodialysis. *Bradley A. Warady, M.D.,* Anna Maria T. Kausz, M.D., Gary Lerner, M.D., Eileen D. Brewer, M.D., Vimal Chadha, M.D., Carlo Brugnara, M.D., Naomi V. Dahl, Pharm.D., Sandra L. Watkins, M.D.; Children's Mercy Hospital, Kansas City, MO; New England Medical Center, Boston, MA; Children's Hospital, Los Angeles, CA; Texas Children's Hospital, Houston, TX; University of Kansas Medical Center, Kansas City, KS; Children's Hospital, Boston, MA; Watson Laboratories, Morristown, NJ; University of Washington Children's Hospital, Seattle, WA.

Presented at the Annual Meeting of the American Society of nephrology, Philadelphia, PA, November 2002.

151E. Assessment of patient and dialysis-related factors associated with hepatitis B vaccine response. *Rowland J. Elwell, Pharm.D.,* Marianne Neumann, R.N., George R. Bailie, Pharm.D., Ph.D.; Albany College of Pharmacy; Albany Dialysis Center, Albany, NY.

Published in Hemodialysis International 2003;7(1):96.

152E. Pharmacokinetics of intraperitoneal cefepime in automated peritoneal dialysis. *Rowland J. Elwell, Pharm.D.,* Reginald F. Frye, Pharm.D., Ph.D., Steven R. Ganchuk, George R. Bailie, Pharm.D., Ph.D.; Albany College of Pharmacy, Albany, NY; University of Pittsburgh, Pittsburgh, PA.

Published in Perit Dial Int 2003;23(Suppl 1):S37.

153E. Pharmacokinetics of oral ciprofloxacin in continuous cycling peritoneal dialysis. *Sharon M. Yeung, B.Sc.Phm.,* Scott E. Walker, M.Sc.Phm., Sandra A.N. Tailor, Pharm.D., Linda Awdishu, B.Sc.Phm., Sheldon Tobe, M.D., Teraiza Yassa, M.D.; Sunnybrook and Women's College Health Sciences Center, Toronto, ON.

Published in Canadian Journal of Hospital Pharmacy, 2003;56(1):66.

Neurology

154E. Cholesterol-lowering effects of divalproex sodium in adult patients with complex partial seizures. *Mahtab Jafari, Pharm.D.,* L. James Willmore, M.D., Patricia Wozniak, Ph.D., Suzanne Giordano, Ph.D., Kenneth Sommerville, M.D.; Abbott Laboratories, Abbott Park, IL; St. Louis University, St. Louis, MO.

Presented at the Annual Meeting of the American Epilepsy Society, Seattle, WA, December 2003.

155E. Cholesterol-lowering effect of divalproex sodium is concentration-related in a monotherapy study of complex partial seizures. Ahmad Beydoun, M.D., *Mahtab Jafari, Pharm.D.,* Patricia Wozniak, Ph.D., Suzanne Giordano, Ph.D., Kenneth Sommerville, M.D.; Abbott Laboratories, Abbott Park, IL; University of Michigan, Ann Arbor, MI.

Presented at the Annual Meeting of the American Epilepsy Society Seattle, WA, December 2003.

156. Accuracy of published methods for predicting unbound phenytoin concentrations. *Mark C. Decerbo, Pharm.D.,* Jingyang Fan, Pharm.D., Timothy F. Lassiter, Pharm.D., M.B.A.; Nevada College of Pharmacy, Las Vegas, NV; Duke University Medical Center, Durham, NC.

PURPOSE: This study examined the predictive abilities of three published equations used in the prediction of actual unbound phenytoin concentrations in hypoalbuminemic patients.
METHODS: Hypoalbuminemic adult patients admitted to a tertiary-care teaching hospital over a one-year period who received phenytoin therapy during their inpatient stay were retrospectively identified. 102 patients with reported free and total phenytoin concentrations from the same blood sample along with a serum albumin value sampled within 48 hours were included. Patients receiving medications known to alter the plasma protein binding of phenytoin and those with renal dysfunction were excluded. Total phenytoin and albumin values were used to predict unbound phenytoin concentrations by three methods. Predicted unbound concentrations were then compared against measured unbound concentrations, and a mean prediction error and root mean squared error were determined to evaluate bias and precision, respectively.
RESULTS: All three equations consistently over-predicted the unbound phenytoin concentration. The mean prediction error for the Sheiner-Tozer equation was 0.53 mg/L (95% CI, 0.43-0.64 mg/L), for the Revised Sheiner-Tozer equation 0.17 mg/L (95% CI, 0.08-0.25 mg/L), and for the Gugler method 0.82 mg/L (95% CI, 0.68-0.96 mg/L). Root mean squared error (RMSE) for each equation was 0.74 mg/L, 0.46 mg/L, and 1.1 mg/L, respectively.
CONCLUSIONS: The Revised Sheiner-Tozer equation exhibited the least degree of bias, and greatest degree of precision of the three equations, as it displayed the smallest respective amounts of prediction error and root mean squared error. However, caution should be utilized as unbound phenytoin concentrations can be over-predicted by all three equations.

157. Efficacy and safety of levetiracetam in pediatric patients with epilepsy: a 2-year follow up. *Collin A. Hovinga, Pharm.D.*; The Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Levetiracetam (LEV) is labeled for the treatment of partial-onset seizures in adults. Currently, there is little data regarding LEV's use in children. This study was to assess the long-term safety and efficacy of LEV in children with pharmacoresistent epilepsy.
METHODS: For children started on LEV between 1/00-1/01, records were reviewed retrospectively to obtain demographics, medical history, LEV dosing and tolerability. Seizure frequency before/after LEV was assessed. Percentage of children with $50% reduction in seizures (RR) and percentage becoming seizure-free were determined

RESULTS: 158 children (10.4 ± 4.6 years) had LEV added to a median of 2 anticonvulsants. 66% of children had partial-onset seizures. After a median of 188 days (1-940) of follow-up, median daily doses were 36.5 mg/kg (6.7-203). Overall median weekly seizure frequency decreased from 7 to 2 (71%; p<0.001). RR and percentage of children becoming seizure-free were 55% and 20%, respectively. Among children with partial-onset seizures, median weekly seizures decreased from 5 to 1.5 (70%; p<0.001) while those with generalized seizures had reductions from 11.6 to 2.3 (80%; p<0.001). LEV monotherapy was achieved in 20% of children and resulted in seizure freedom in 45%. Adverse events occurred in 34% of children and resulted in LEV discontinuation in 55%. Common side effects were somnolence/sedation (13%), psychiatric-related/worsening of behavior (17%), and increased seizure frequency (8%).
CONCLUSIONS: These results suggest LEV is effective in treating both partial and generalized seizures in children. LEV monotherapy can be effective in children refractory to other anticonvulsants. Side effects tended to be CNS- and behaviorally-related.

Nutrition

158. Evaluation of weight control-related knowledge, attitudes, and practice among customers in a community pharmacy in Taipei. Tien-Yuan Wu, B.S., Ya-Wen Lee, B.S., Wei-Yu Chen, B.S., Yu-Ching Chou, B.S., *Hsiang-Yin Chen, M.S., Pharm.D.*; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: This study was designed to evaluate the knowledge, attitudes, and practice towards weight control among customers visited a community pharmacy in Taiwan.
METHODS: A total number of 502 participants who came to Yes-Chain Pharmacy were sampled from August 12th to September 4th, 2002. The participants were asked to answer a validated questionnaire with three sections. The first section contained 10 dichotomous questions to assess the level of knowledge. Both of the second and third sections contained with 10 questions in a 5- point scale to estimate the attitudes and practice. The weight, body fat, and waist circumference of the participants were also documented.
RESULTS: Out of 502 participants, 424 were completed with a completion rate of 84.5 %. Most of participants showed lack of appropriate knowledge related to weight control with a mean score of 3.45 ± 2.24, especially about general concept with a mean score of 0.76±0.78 compared with a perfect score of 10. One interesting finding is that the mean scores are significantly low among populations with cigarette (p=0.001) and alcohol consumption (p<0.001). Average attitudes score was 38.80 ± 5.70 for all respondents, and 39.39 ± 5.59 and 37.80 ± 5.78 for non-obese and obese groups, respectively (p<0.05). The mean score of practice was 20.92 ± 6.14 for all respondents, and 20.59 ± 5.93 and 21.49 ± 6.46 for non-obese and obese groups.
CONCLUSIONS: Health care professionals should take a more active role to provide education of weight control in Taiwan, especially among populations with cigarette and alcohol consumption. Further studies should be conducted to assess the long-term effects of education on practice change.

159. Risk factors for developing catheter-related infections with home TPN use. *Kimberly E. Thomas, Pharm.D.,* John K. Siepler, Pharm.D., Jeffrey H. King, Pharm.D.; University of California Davis Medical Center, Sacramento, CA.

PURPOSE: To assess characteristics that put patients receiving home TPN at risk for developing catheter-related infections.
METHODS: This was a retrospective review of all UC Davis Medical Center patients who received home TPN between February 2002 and January 2003. Patients were compared for differences in characteristics including age, gender, tobacco use, catheter type, indication for starting TPN, and duration of TPN use.
RESULTS: Home TPN therapy was used by 47 patients from our institution during this time period. There were 6,782 total catheter days studied resulting in 15 infections in 13 different patients for a total of 2.2 infections/1000 catheter days. Pediatric patients developed 2.5 ± 2.8 infections/1000 catheter days and adult patients developed and 2.1 ± 3.6 infections/1000 catheter days. There was no difference between the genders or between smokers and non-smokers. Patients who received TPN through a PICC developed 2.6 ± 3.6 infections/1000 catheter days while patients who received TPN through a Broviac/Hickman catheter developed 1.9 ± 4.4 infections/1000 catheter days. Patients started on TPN due to perforated bowel or fistula, pancreatic disease, enteritis, short bowel, or bowel obstruction developed 4.2 ± 5.3, 4.0 ± 4.0, 2.0 ± 5.7, 1.2 ± 2.0, and 1.0 ± 1.0 infections/1000 catheter days, respectively. Patients receiving long-term therapy developed 1.0 ± 2.1 infections/1000 catheter days while patients receiving short-term therapy developed 3.1 ± 3.7 infections/1000 catheter days. No differences were statistically significant.
CONCLUSIONS: This data shows some trends that could become significant with a larger number of patients. Young patients may have increased risk for developing catheter-related infections than older patients and patients on long-term therapy may have decreased risk for developing catheter-related infections.

160E. Energy requirements of non-ambulatory tube-fed adult patients with cerebral palsy and chronic hypothermia. *Roland N. Dickerson, Pharm.D.,* Rex O. Brown, Pharm.D., Debra L. Hanna, M.D., John E. Williams, M.D.; University of Tennessee Health Science Center, Memphis, TN; Arlington Developmental Center, Arlington, TN.

Published in JPEN 2003;27:S36.

161. A nationwide survey of long-term care facilities to determine the characteristics of medication administration through enteral feeding catheters. *Charles F. Seifert, Pharm.D., FCCP,* Barbara A. Johnston, Ph.D., R.N.; Texas Tech University Health Sciences Center, Lubbock, TX.

BACKGROUND: Our previous data clearly showed tremendous differences in nursing practices and techniques within the State of Texas regarding the administration of medications through enteral feeding catheters between long-term care facilities that predominantly serve a rural versus an urban population.
PURPOSE: To determine the incidence and characteristics of medication administration through enteral feeding catheters in the long-term care setting in the United States with particular emphasis on the delineation between practices in facilities that predominantly serve a rural versus an urban population.
METHODS: A 36-item validated survey was mailed to the Directors of Nursing of the 16,517 long-term care facilities registered with the U.S. Medicare long-term care facility database registry.
RESULTS: The first 1116 (6.8%) surveys were included in this analysis. The majority of nurses responding were RNs (93%), with extensive years of experience (19 years), working in facilities predominantly serving a rural area (57%). There were significant differences between rural and urban facilities with regard to the percent of patients receiving medications through EFCs (6.8% vs 8.6%, p<0.0001), number of oral medications/day (8.5 vs 9.6, p<0.0001), amount of flush before and after administering medications (64 ml vs 59 ml, p=0.0207) and those attending a seminar/inservice (45% vs 58%, p<0.0001). Medication obstruction rate was significantly increased when nurses used 3 or more inappropriate techniques (8.3% vs 4.8%, p=0.0025) particularly crushing enteric-coated (9.0% vs 4.6%, p=0.0001) and sustained-release dosage forms (8.6% vs 4.7%, p=0.0004).
CONCLUSIONS: A universal set of guidelines to administer medications through EFCs should be adopted and widely disseminated particularly to LTCF in rural areas.

162. Which medications clog nasoduodenal feeding tubes? *Kamila A. Dell, Pharm.D., BCPS,* Nick Lonardo, Pharm.D., Jeanne Klimo, Pharm.D., BCPS; University of Utah Hospitals and Clinics, Salt Lake City, UT.

OBJECTIVE: To investigate which commonly administered medications used in critical care clog nasoduodenal feeding tubes.
METHODS: Nasoduodenal tubes (8 French Dobbhoff® tubes) were set up in a 37°C water bath to simulate the in vivo environment. All medications were tested with two feeding formulas, Promote® (1 kcal/ml) and Nepro® (2 kcal/ml). The administration procedure consisted of stopping tube feeding formula, flushing the nasoduodenal tube (NDT) with 30 ml of water, administering the medication, flushing with 30 ml of water, and resuming the tube feeding. Each medication was tested 3 times with both feeding formulas. The medications were administered consecutively until a clog occurred. Attempts were made to dislodge the clog by using warm water and, if ineffective, an alkalinized method. All medications that clogged the NDT were retried in new NDT.
RESULTS: This study tested 87 medications chosen by critical care pharmacists. Of all medications tested, only 3 clogged the NDT: aspirin tablet, sertraline liquid, and clarithromycin suspension. Retesting in new NDT resulted in no clogs. During administration, the medication can back up into the tube feeding tubing and mix with the feeding formula, which could alter the properties of the medications. Both aspirin and sertraline caused the feeding formulas to curdle, possibly leading to NDT occlusions.
CONCLUSIONS: Medications do not appear to clog NDT when administered through new NDTs, but the cumulative administration of medications, which occurs in practice, can cause NDT clogs. Residue from the tube feeds and/or medications, along with curdling of the tube feeds, contribute to NDT clogs.

Oncology

163E. Management of chemotherapy-induced febrile neutropenia (FN) with colony-stimulating factor (CSF): a meta-analysis. *Otavio Clark, M.D.,* Benjamin Djulbegovic, M.D., David Dale, Jeffrey Crawford, Gary H. Lyman, the ANC Study Group; Institute of Radium, Campinas, Brazil; H. Lee Moffitt Cancer Center, Tampa, FL; University of Washington Medical Center, Seattle, WA; Duke University Medical Center, Durham, NC; University of Rochester Medical Center, Rochester, NY.

Presented at the Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 31, 2003.

164E. Intermittent bolus dosing (weekly infusions) with a liposome-encapsulated c-raf antisense oligodeoxynucleotide (LErafAON) in patients with advanced solid tumors: a phase I study. Chao Hui Huang, Charles M. Rudin, John Marshall, *Christina Fleming,* James Hwang, Chuanbo Zhang, Deepak Kumar, Prafulla Gokhale, Usha Kasid, Mark J. Ratain; Temple University, Philadelphia, PA; University of Chicago Hospitals, Chicago, IL; Georgetown University Medical Center, Washington, DC; NeoPharm, Inc., Lake Forest, IL.

Presented at the Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 31-June 3, 2003.

165E. Economic burden of seven tumors by course of therapy and treatment failure. *Lucie Kutikova, Ph.D.,* Lee Bowman, Ph.D., Stella Chang, M.P.H., Stacey Long, M.S.; Eli Lilly and Company, Indianapolis, IN; MEDSTAT Group, Washington, DC.

Presented at the Annual Meeting of ECCO 12, Copenhagen, Denmark, September 21-25, 2003.

166. A retrospective analysis evaluating the cost-effectiveness of reduced-dosage ondansetron in the prevention of postoperative nausea and vomiting. *David M. Baribeault, R.Ph, BCOP,* Glynne Stanley, M.D., Pam Badger, R.N.; Boston Medical Center, Boston, MA.

PURPOSE: This study evaluated the cost-effectiveness of a 1mg intravenous of dose ondansetron for the prevention of postoperative nausea and vomiting (PONV) as compared with the previously utilized 4mg intravenous dose.
METHODS: Two groups of patients undergoing ambulatory surgery at Boston Medical Center were identified for chart review. The control group was all patients treated during the period from January 2002 to June 2002. This group of patients was treated before the anesthesia department adopted a practice of utilizing a 1mg dose of intravenous ondansetron to prevent PONV. The preventative dose of ondansetron used in this group was 4mg intravenously. The treatment group was those patients treated from July 2002 to December 2002. The preventative dose of ondansetron used in this group was 1mg intravenously. The primary end-point was rates of adequate prophylaxis as defined by any need for nausea rescue medications during the postoperative observation period. The secondary end-point was the cost of ondansetron utilized during those time periods.
RESULTS: The total number of ambulatory procedures performed during each time period was quite similar. Both groups were similar with respect to demographics and surgery type. The overall need for rescue medication administration was essentially the same (13% vs 13.4%, p>0.85) while the overall utilization of ondansetron was decreased by approximately 30%.
CONCLUSIONS: Reduced dosages of intravenous ondansetron provide adequate treatment for the prevention of PONV at a much lower cost.

167E. Pharmacokinetics of irinotecan and the proteasome inhibitor bortezomib in adult patients with solid malignancies. *Darrell J. Nix, Ph.D.,* J. Paul Eder, M.D., Thomas J. Lynch, M.D., Nela Belonogovna, M.D., Roberto Guerciolini, M.D., James C. Cusack, M.D., David P. Ryan, M.D., Jeffrey G. Supko, Ph.D.; Millennium Pharmaceuticals, Inc, Cambridge, MA; Harvard Medical School, Boston, MA.

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168. Community experience with filgrastim in diverse non-myeloid malignancies: An open-label phase 4 study. *James M. Epstein, M.D.,* Sheila M. Donnelly, M.D., Joan M. O'Byrne, M.S., Brian W. McGuire, Ph.D., Jimmie H. Harvey, M.D.; Missouri Baptist Cancer Center, St. Louis, MO; Heywood Hospital, Gardner, MA; Amgen, Inc., Thousand Oaks, CA; Birmingham Hematology/Oncology, Birmingham, AL.

PURPOSE: A phase 4 trial of 99 community oncology practices was conducted to study filgrastim, a recombinant growth factor, in chemotherapy-induced neutropenia.
METHODS: Any non-myeloid malignancy and chemotherapy regimen were allowed. Filgrastim was started 24 hours after chemotherapy in all cycles, to a post-nadir ANC ≥ 10 x 10^9/L. Blood counts were to be taken at least twice per week. Endpoints included incidence and duration of neutropenia and percent of cycles given on time at planned dose.
RESULTS: A total of 3197 cycles were delivered across 780 patients representing 33 different tumor types. Median (range) age was 58 (< 1, 91); 64% were female. Mean number of filgrastim doses per cycle was 11.2 (SD 3.5) and varied little across cycles. Some variation was seen between tumor types, reflecting the differing intensities of chemotherapy.

		Days of filgrastim	
Tumor type	Cycles	Mean (SD)	Median
Breast	1012	11.0 (2.8)	10.5
NSCLC	327	10.6 (3.0)	10.0
SCLC	398	10.7 (3.1)	10.0
Ovarian	309	11.5 (3.1)	11.0
NHL	466	11.2 (3.5)	10.0
Other	572	12.0 (4.7)	11.0
All tumor types	3084	11.2 (3.5)	11.0

Patients < 18 years of age were significantly more likely to require a longer duration of filgrastim dosing (mean 14.4 days, SD 4.4). Grade 4 neutropenia was observed in 17% of patient-cycles, although mean duration was short (0.4 days, SD 1.1). A high proportion of chemotherapy cycles were at full dose (90%) and on time (91%).
CONCLUSIONS: Filgrastim facilitated planned delivery of chemotherapy with a low rate of neutropenic complications when used as labeled.

169. Medication-use evaluation study of usage and clinical outcomes of erythropoietic agents for chemotherapy-induced anemia in clinical practice. *Robert Adamson, Pharm.D.,* Dianne Tomita, M.P.H., Bradley Stolshek, Pharm.D.; Saint Barnabas Healthcare System, Livingston, NJ; Amgen Inc., Thousand Oaks, CA.

PURPOSE: To compare initial usage and clinical outcomes of darbepoetin alfa (DA; Aranesp®) to epoetin alfa (EPO) for chemotherapy-induced anemia (CIA) in routine oncology practice.
METHODS: Eleven community and five hospital oncology clinics abstracted dosing and hemoglobin data from consecutive medical charts of patients with CIA on 01 April–31 July 2002 (EPO) and 01 August-04 October 2002 (DA). Thirteen weeks of chart data were analyzed using descriptive statistics. Both intent-to-treat (ITT) and available data approaches were used. For ITT, missing hemoglobin values were imputed using last-value-carried-forward; for available data, no imputation was used. For both, hemoglobin values within 28 days of a transfusion were excluded.
RESULTS: Data were collected on 1391 (752 DA; 639 EPO) patients; 735 and 558 patients received only DA or EPO, respectively; the remainder received both agents. The most frequently administered initial doses were DA 200 µg every 2 weeks (DA200Q2W; 75%) or EPO 40,000 U weekly (EPO40KQW; 74%). For those who received the most common doses, the mean hemoglobin change from baseline after 12 weeks was 1.0 g/dL for both agents (ITT) and 1.3 g/dL and 0.9 g/dL for DA and EPO, respectively (available). In these patients, 11% of DA and 14% of EPO patients received a dose increase at a median of 7 weeks. The incidence of transfusions was also comparable (DA, 8% vs EPO, 9%).
CONCLUSIONS: Darbepoetin alfa 200 µg Q2W achieves comparable clinical outcomes to EPO40KQW and has been adopted as the standard regimen for CIA in clinical practice.

170. The influence of St. John's wort on the pharmacokinetics and protein binding of imatinib mesylate. *Julie M. Bullock, Pharm.D.,* Patrick F. Smith, Pharm.D., Curt Haas, Pharm.D., Brent M. Booker, Pharm.D., Charles Berenson, M.D., William J. Jusko, Ph.D.; University at Buffalo; WNY VA Health System Clinical Research Center; Roswell Park Cancer Institute, Buffalo, NY.

PURPOSE: Imatinib, an oral tyrosine kinase inhibitor approved for chronic leukemia, is metabolized by cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (PgP), making it potentially susceptible to significant drug interactions, including St. John's Wort (SJW), a commonly used herbal product which induces these enzymes.
METHODS: An 18-day, open-label, complete crossover, fixed sequence study in 10 healthy volunteers evaluated the impact of SJW on imatinib PK. Single 400 mg imatinib doses were administered before and after 15 days of SJW 300 mg TID. Twelve plasma concentrations for total imatinib were determined by a validated LC/MS/MS assay (CV<5%) over 48 hours before and after SJW; free concentrations measured at 3 and 24 hours. Pharmacokinetic parameters were determined by non-compartmental analysis, and statistical comparisons were made by the paired t-test (log-transformed data), and bioequivalence was evaluated for AUC and C_{max}.
RESULTS: Administered alone, the median (range) imatinib $AUC_{0-\infty}$ C_{max}, and half-life were 28.9 (13.4-36.7) µg*hour/ml, 1.80 (0.88-2.6) ng/ml, and 13.5 (10.8-18.1) hours, respectively. The PK of imatinib was significantly altered by SJW: the median $AUC_{0-\infty}$ C_{max}, and half-life were reduced by approximately 32%, 29%, and 21% (p<0.005 for all). PB ranged from 97.7-90.3% (mean 94.9%), was concentration independent, and was not altered by SJW. Both AUC and C_{max} failed the bioequivalence test. No adverse events were reported during the study.
CONCLUSIONS: SJW significantly reduced imatinib exposure due to induction of hepatic metabolism and reduced absorption likely thru both CYP3A4 and PgP. Imatinib therapeutic outcomes depend upon the maintenance of adequate drug concentrations, thus coadministration of SJW may significantly compromise the clinical efficacy of imatinib therapy.

171E. Most patients treated with adjuvant chemotherapy for breast cancer receive substantially reduced dose intensity: Results of practice pattern survey of nearly 20,000 patients. *Olayemi Agboola, M.S.,* Jeffrey Crawford, M.D., David Dale, M.D., Gary H. Lyman, M.D., M.P.H.; University of Rochester, Rochester, NY; Duke University Medical Center, Durham, NC; University of Washington, Seattle, WA.

Presented at the Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 31, 2003.

172E. A single pegfilgrastim dose per cycle supports dose-dense (q14d) CHOP-R in patients with NHL. *Timothy D. Moore, M.D.,* Taral Patel, M.D., Mark L. Segal, M.D., Jeffrey Zangmeister, M.D., Tarek A. Chidiac, M.D., Ralph W. Roach, M.D., Mark E. Thompson, M.D., Nye R. Larrimer, M.D.; Mid-Ohio Oncology/Hematology, Columbus, OH.

Published in Blood 2002;100:(Abstract #2245).

173. A bloody battle: darbepoetin and epoetin use in oncology. *Maureen E. Haas, Pharm.D.*; Hollings Cancer Center; Medical University of South Carolina, Charleston, SC.

PURPOSE: Identify if using either epoetin alfa weekly or darbepoetin alfa every other week would achieve and maintain hemoglobin levels at the desired concentration. Assess financial impact of each agent.
METHODS: From January 2003 through June 2003 patients prescribed either epoetin alfa or darbepoetin alfa for cancer related anemia were identified. Baseline demographic data in addition to: Cancer type, chemotherapy regimen, product selected, dose, duration, hemoglobin, hematocrit, iron and ferritin level and supplementation were obtained. Data was recorded with subsequent doses as available and assessed at baseline, four, eight, and twelve weeks. Financial impact to the pharmacy was calculated based on number of patient visits, purchase price, and subsequent reimbursement to the institution.
RESULTS: Preliminary data identified 130 patients. Ninety-four orders for epoetin alfa 40,000 Units weekly obtained an average hemoglobin of 10.66 Gm/dL (SD +1.24). Twenty-three orders for darbepoetin 200 µg every other week obtained an average hemoglobin of 10.70 Gm/dL (SD +1.38). Epoetin alfa 40,000 and 60,000 Units obtained hemoglobin ≥ 12 Gm/dL in 28/94 (30%) and 5/11 (45%) patients. Darbepoetin 200 and 300µg achieved goal hemoglobin in 5/25 (20%) and 1 of 2 (50%) patients. Completed results including average documented increase from baseline in hemoglobin at four, eight, and twelve week endpoints and financial reimbursement will be reported after data completion in August 2003.
CONCLUSIONS: Both epoetin alfa weekly and darbepoetin alfa every other week appear to achieve similar hemoglobin levels in this patient population. These results will provide data to support implementation of clinical prescribing guidelines based on efficacy and cost at our institution.

174. Less frequently administered darbepoetin alfa is comparable to epoetin alfa for the treatment of chemotherapy-induced anemia: a pooled analysis of multicenter clinical trials conducted in the United States. *Cynthia S. Headlee, R.P.H.,* Barry C. Mirtsching, M.D.; Center for Oncology Research and Treatment, Dallas, TX.

PURPOSE: To evaluate the relative efficacy of darbepoetin alfa (DA; Aranesp®) administered every 2 weeks (Q2W) and epoetin alfa (EPO) administered weekly (QW) or three times weekly (TIW) in clinical trials.
METHODS: A combined analysis of individual patient data from 3 similarly designed US multicenter trials was performed. Patients with anemia (hemoglobin [Hgb] ≤ 11 g/dL) and non-myeloid malignancies undergoing chemotherapy were eligible for the studies included in the analysis. Patients in the DA group (n=1206) received 3.0 µg/kg Q2W. EPO patients (n=115) received 150 U/kg QW or 40,000 U QW; both groups exhibited similar responses and were combined for this analysis.
RESULTS: Excluding Hgb values within 28 days of transfusion, mean Hgb changes from baseline after 4, 8, and 12 weeks were comparable (DA: 0.4, 1.0, and 1.4 g/dL vs EPO: 0.5, 1.1, and 1.4 g/dL, respectively; intent-to-treat approach) among patients with a valid baseline Hgb value. The Kaplan-Meier proportion of patients with a hematopoietic response (≥ 2-g/dL Hgb increase or Hgb ≥ 12 g/dL) was also comparable (DA: 71% vs EPO: 71%). The incidence of transfusions from weeks 5 to 12 was 18% (DA) and 14% (EPO) among patients who completed the study at least through study day 29.
CONCLUSIONS: Darbepoetin alfa 3 µg/kg Q2W appears to be as effective as EPO in treating chemotherapy-induced anemia, with the added benefit of less frequent administration.

175. Evaluation of patient satisfaction with chemotherapy education in a gynecology oncology center. *Judith A. Smith, Pharm.D., BCOP,* Catherine Kindo, Pharm.D., Shiney Kurian, R.N., Lynn M. Whitaker, R.N., Catherine Burke, R.N., Brandi Wachel, R.N., Charolette C. Sun, D.PH., Candice L. Weaver, B.S., Martha G. Danielson, Pharm.D., Mary Fitzgerald, B.S., Mark Munsell, M.S., Frances A. Zandstra, B.S.N., M.B.A., Diane C. Bodurka, M.D.; M.D. Anderson Cancer Center, Houston, TX.

PURPOSE: To assess patient preferences for receiving chemotherapy education provided by a health care team in an outpatient clinic setting and identify any unmet needs regarding patient chemotherapy education.
METHODS: A total of seventeen questions were developed to elucidate the baseline patient satisfaction on chemotherapy education. After signing into clinic, patients were offered a copy of the study patient questionnaires, with a cover letter describing the study objective.
RESULTS: 282 questionnaires were completed and 190 participants had previously received chemotherapy, and excluded those that had not received chemotherapy from the study. Of the 165 participants that were previously treated at our institution, a total of 66.7% (110/165) had received some form of chemotherapy education specifically from our clinic. The majority of patients reported that they preferred to receive information about their chemotherapy via written materials and/or through a conversation with a health care professional. Regardless of the source of information, 62.6% (119/190), of patients felt they were provided with adequate information about their chemotherapy treatment. 42.4% of patients reported that they would like more information about their chemotherapy; however the majority of patients (57.6%) either did not want or were unsure if they needed additional information.
CONCLUSIONS: A health care professional reviews the information with the patient prior to obtaining consent to receive chemotherapy. The data revealed that our current practice is consistent with our patients' preferences. However, this survey did identify new information that patients want to know about chemotherapy such how chemotherapy works, why chemotherapy stops working, and drug-drug as well as drug-food interactions. This information will be incorporated into the patient education materials.

Pediatrics

176E. An open-label trial of Adderall® XR: quality of life assessments. Floyd R. Sallee, M.D., Ph.D., Paul J. Ambrosini, M.D., Frank A. Lopez, M.D., Simon J. Tulloch, M.D., M. Alex Michaels, M.D., *Chris Paap, Pharm.D., FCCP, BCPS*; Cincinnati Children's Hospital and Medical Center, Cincinnati, OH; MCP Hahnemann, Philadelphia, PA; Shire US Inc., Newport, KY.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003

177E. An open-label, community-assessment trial of Adderall® XR in pediatric attention deficit hyperactivity disorder. Paul J. Ambrosini, M.D., Frank A. Lopez, M.D., Mark C. Chandler, M.D., Simon J. Tulloch, M.D., M. Alex Michaels, M.D., *Chris Paap, Pharm.D., FCCP, BCPS*; MCP Hahnemann, Philadelphia, PA; North Carolina Neuropsychiatry, Chapel Hill, NC; Shire US Inc., Newport, KY.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003.

178E. Effect of anesthesia on oxygenation during newborn circumcision. *Victoria Tutag Lehr, Pharm.D.,* Eugene Cepeda, M.D., J.V. Aranda, M.D., Ph.D., Ron Thomas, Ph.D., Sharada Shree, M.M.B.S.; Wayne State University; Children's Hospital of Michigan, Detroit, MI.

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179E. Conditioning of blood prime using Diapact®-based continuous hemodialysis for pediatric patients. *Deborah A. Pasko, Pharm.D,* Theresa A. Mottes, R.N., Bruce A. Mueller, Pharm.D, FCCP, BCPS; University of Michigan, Ann Arbor, MI.

Presented at the 8th International Conference on Continuous Renal Replacement Therapies, San Diego, CA, March 6, 2003.

180. Tobramycin pharmacokinetics in febrile neutropenic children undergoing stem cell transplantation: once vs three times daily administration. *L. Lee Dupuis, M.Sc.Phm., FCSHP,* Lillian Sung, B.A., M.D., FRCPC, Tracey Taylor, B.Sc.Phm., Mohammed Abdolell, B.Sc., M.Sc., Upton Allen, M.D., FRCPC, John Doyle, M.D., FRCPC, Anna Taddio, B.Sc.Phm., Ph.D.; The Hospital for Sick Children; University of Toronto; Cancer Care Ontario, Toronto, ON, Canada.

PURPOSE: Validated pediatric q24h aminoglycoside dosing guidelines are not available. This study describes the pharmacokinetic disposition of IV tobramycin in children undergoing stem cell transplant (SCT) following either q8h or q24h administration. This information was used to create initial q24h dosing guidelines for this population.
METHODS: In this randomized, double-blind, controlled study, children undergoing SCT received tobramycin either q8h (2.5 mg/kg/dose) or Q24H (<5 years: 9 mg/kg/dose; 5-<12 years: 8 mg/kg/dose; ≥12 years: 7 mg/kg/dose). Serum tobramycin concentrations were obtained 2 and 8 hours after the first dose. Parameters were calculated using first order, one-compartment equations. Initial q24h dosing guidelines were derived using the parameters from all children to achieve a maximum serum concentration (C_{max}) of 20-22.5 mg/L and a drug free interval (time during dosing interval where concentration < 1mg/L) of at least 4 hours.
RESULTS: 60 children were enrolled. Tobramycin concentrations were obtained immediately after the first dose in 45 children (mean age: 6.3 years; range: 0.6-16.6 years). Mean tobramycin pharmacokinetic parameters (± SD) following the first dose are shown in the table.

	N	Ke (hr^{-1})	Vd (L/kg)	C_{maxss} (mg/L)	AUC (mg/L•hour)	Drug-free interval (hours)
Q8H	23	0.34 ± 0.094	0.48 ± 0.207	5.8 ± 1.80	28.3 ± 8.19	2.6 ± 1.14
Q24H	22	0.43 ± 0.115	0.43 ± 0.257	17.8 ± 7.19	55.8 ± 18.96	16.6 ± 2.10

Tobramycin Vd varied with age. Initial q24h tobramycin doses recommended to achieve the target parameters are: <5 years: 10 mg/kg/dose; 5-<9 years: 13 mg/kg/dose; 9-<12 years: 8 mg/kg/dose; and ≥12 years: 6 mg/kg/dose.
CONCLUSIONS: Children undergoing SCT who receive tobramycin q24h should receive initial doses based on age; subsequent doses should be individualized based on tobramycin concentrations. Further validation of the proposed dosing guidelines is required.

Pharmacoeconomics

181. Cost-effectiveness of bimatoprost 0.03% versus travoprost 0.004% for glaucoma. *Jeffrey T. Lee, Pharm.D.,* John G. Walt, M.B.A.; Allergan Global Health Outcomes Strategy and Research, Irvine, CA.

OBJECTIVES: To evaluate and compare the yearly cost-effectiveness of the two newer lipid class of topical medications in the treatment of glaucoma, bimatoprost 0.03% and travoprost 0.004%.
METHODS: A pharmacoeconomic decision-tree model was constructed based on a six-month randomized controlled efficacy-trial comparing bimatoprost 0.03%, a prostamide (AWP of $55.79) and travoprost 0.004% a prostaglandin (AWP of $55.75). The trial evaluated the percent of patients achieving a range of target intraocular pressures (IOPs). The cost of treatment to achieve target was calculated as the average total yearly medication and treatment cost/expected effectiveness based on patients achieving a specific target IOP. A weighted average cost-effectiveness ratio was calculated based on the actual distribution of target IOPs set for patients on lipid monotherapy in a separate study. Cost-effectiveness was based on six months of the actual trial treatment linearly extended to one year.
RESULTS: With bimatoprost, 86% of patients reached and maintained a target IOP of <17 mm Hg measured at 9 AM at six-months vs 50% of patients with travoprost. The one-year cost-effectiveness ratios (at <17 mm Hg) were $1,201 vs $2,411 per successful patient on bimatoprost vs travoprost. Average cost-effectiveness ratios based weighted range of target IOPs were $2,428 vs $4,551, for bimatoprost vs travoprost. In an analysis of incremental cost-per additional treatment success (ICER), bimatoprost dominated travoprost.
CONCLUSIONS: Due to a greater percentage of glaucoma patients achieving target treatment goals set by ophthalmologists (considered effectiveness) with bimatoprost 0.03%, bimatoprost monotherapy has a more favorable cost-effectiveness profile than travoprost.

182. Evaluating the costs and benefits of collaborative drug therapy management (CDTM) in a community health center network. *Daniel J. Melzer, Pharm.D.,* Kem P. Krueger, Ph.D., Pharm.D., Paul D. Brackett, Pharm.D.; Columbus Regional Healthcare System, Columbus, GA; Auburn University, Auburn, AL.

PURPOSE: This study documented collaborative drug therapy management (CDTM) in community health network to (1) determine if CDTM improves clinical outcomes and (2) determine if CDTM is cost-effective. To date, the cost-effectiveness of CDTM in community health network has not been established.
METHODS: Patients with diabetes, hypertension, and/or hyperlipidemia were referred for pharmacy clinical services by their primary care provider. A cost-effectiveness analysis was performed on the costs of a clinical pharmacist added to the current care of patients. In addition, clinical outcomes of HbA_{1c}, BP, LDL, and urgent care utilization were collected and analyzed.
RESULTS: CDTM at 6 months produced the following results: (mean decrease from baseline) HbA_{1c} 3.0%, SBP 8 mm/Hg, DBP 6.9 mm/Hg, and LDL 29.6 mg/dL (all $p<0.05$ except LDL); 38 % and 83 % of patients were at BP and LDL goals respectively (both $p<0.05$); and less utilization of ED visits (6 vs 1). The total net cost of the clinical pharmacist to the Community Health Center is $5580 over six months.
CONCLUSIONS: CDTM improves clinical outcomes which resulted in less utilization of urgent care. CDTM incurred a small increase in cost of standard care, and a fee of $32 per clinical pharmacy visit would make CDTM cost-neutral. Continuation of this study along with increased patient enrollment and longer time frame may strengthen the evidence for benefits of CDTM.

183. Cost effectiveness of nesiritide in patients treated for congestive heart failure. *Herbert E. Pettit, Pharm.D., BCPS,* Alexander M. Carrick, B.S.; Central Baptist Hospital, Lexington, KY.

PURPOSE: This study compared the total cost effectiveness of nesiritide therapy in patients with documented congestive heart failure versus case controls.
METHODS: The first 20 records were reviewed from February 1-July 31, 2002 for discharged patients with APR-DRG 194 congestive heart failure having received nesiritide. These were matched with 20 non-nesiritide patients based on severity of illness, ICU length of stay, and age. Patients undergoing operative procedures were excluded. Variables compared were: Population parameters, length of stay, ejection fraction, 30 day readmission, concurrent medication, and total admission cost.
RESULTS: There were no statistical differences in the populations for the nesiritide vs the non-nesiritide groups with respect to: severity of illness, ICU days (days ± SD) 0.8 ± 1.2 vs 0.4 ± 0.9, age (years ± SD) 70.0 ± 11.3 vs 71.9 ± 10.9, ejection fraction (% ± SD) 39.6 ± 19.3 vs 45.3 ± 16.0, 30 day readmission 15% vs 10%, and concurrent medication. Total admission cost was $5608 ± 3637 vs $4347 ± 1696. In the nesiritide group the mean length of infusion was (hours ± SD) 46.6 ± 27.1 utilizing (1.5 mg vials ± SD) 2.4 ± 1.1 of nesiritide. Statistical difference was found in length of stay (days ± SD) 5.4 ± 2.7 vs 3.8 ± 1.3 ($p<0.05$).
CONCLUSIONS: Despite finding no statistical difference in total admission cost, there was an actual total cost difference, bringing into question the cost effectiveness of nesiritide therapy. Further study is warranted.

184E. Dose conversion of erythropoietic agents in chemotherapy-related anemia: a meta-analysis. *James Rosberg, M.B.A., Ph.D.,* Eric Wu, Ph.D., John Fastenau, M.P.H., R.Ph., Catherine Tak Piech, M.B.A.; Analysis Group, Inc., Boston, MA; Ortho Biotech Products, LP, Bridgewater, NJ.

Presented at the 8th International Meeting of the International Society for Pharmacoeconomic and Outcomes Research, Arlington, VA, May 18-21, 2003.

185. Determination of the costs associated with the inpatient treatment of infections caused by macrolide-resistant *Streptococcus pneumoniae*. Donald G. Klepser, M.B.A., Ph.D. candidate, Michael E. Klepser, Pharm.D.; University of Iowa, Iowa City, IA; Ferris State University, Big Rapids, MI.

PURPOSE: The objective of this study was to examine costs associated with health care resource utilization among inpatients infected with macrolide resistant *S. pneumoniae*.
METHODS: 231 patients infected with *S. pneumoniae* and hospitalized between January 1995 and December 1998 were included. An intervention window was defined as the day the specimen for the first positive culture was obtained through the seventh day after this event. Patient demographics, baseline clinical characteristics, and cost data over the intervention window were compared between the susceptible and non-susceptible groups. Cost data (total inpatient, room, nursing, pharmacy, and laboratory) were analyzed using Wilcoxon rank sums. Analyses were also conducted with matched data.
RESULTS: 48/231 patients were infected with macrolide non-susceptible isolates. Patients in the non-susceptible group were younger (mean age 34.5 vs 46.5 years, $p<0.05$), had fewer bloodstream isolates (19% vs 40%, $p<0.05$), and had a higher rate of pre-admission antibiotics (81% vs 60%, $p<0.05$). Median, per patient, total costs associated with the treatment in the macrolide-susceptible and non-susceptible groups were $8,562.00 and $9,734.00 ($p=0.38$), respectively. A significant difference in room costs was detected between the groups (susceptible = $2,997.00 vs non-susceptible = $3,693.00, $p=0.0075$). Analysis with matched data revealed no significant differences between groups, however, total, room, and nursing costs differences trended toward significantly higher costs in the non-susceptible group ($p=0.2$, 0.06, 0.17).
CONCLUSIONS: Macrolide resistance negatively impacts costs associated with patient management. Efforts to minimize the cost to the institution should focus on initiating appropriate empiric therapy and early transition to outpatient management.

186E. Individual and societal consequences of non-antibiotic treatment of strep throat. Alan Salkind, M.D., *Julie Wright, Pharm.D.*; University of Missouri at Kansas City, Kansas City, MO.

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187. Factors affecting the costs of an intensive care unit day: Implications for pharmacoeconomic studies. *Craig S. Roberts, Pharm.D., M.P.A.,* Joseph F. Dasta, M.Sc., Sally R. Kim, M.P.H., Trent P. McLaughlin, Ph.D., Samir H. Moody, Pharm.D., M.B.A., Catherine Tak Piech, M.B.A.; NDCHealth, Yardley, PA; Ohio State University, Columbus, OH; NDCHealth, Phoenix, AZ; Ortho Biotech Products, L.P., Bridgewater, NJ.

PURPOSE: Although pharmacoeconomic studies often use length of stay as an endpoint, there are few data about the cost of intensive care unit (ICU) care. This study estimated the daily cost of ICU care and examined variables affecting this cost.
METHODS: Data were collected on adult ICU patients between 10/01/02 – 12/30/02 from over 250 hospitals. Patients were classified as trauma, surgical, or medical. ICU days were identified using hospital charges, and daily costs were calculated as the sum of daily charges multiplied by the hospital-specific cost-to-charge ratio. The effect of variables on cost was examined using log-linear regression, including covariates of ICU day, admission type, mechanical ventilation, and patient and hospital characteristics.
RESULTS: 51,009 patients had a mean (SD) age of 62.3 years (17.1) and 53.3% were male. Mean cost and hospital length of stay were $32,253 ($45,818) and 10.7 days (13.0) Patients were in the ICU a mean of 4.3 days (6.7) with a total mean ICU cost of $19,725 ($31,778). Mean daily ICU costs were highest on the first ICU day, $7,728 ($8,509); decreased on day two to $3,872 ($4,223); and became stable from day 3 forward, at $3,436 ($3,550). Adjusting for patient and hospital characteristics, ICU costs were significantly greater for males ($p<0.001$), surgical and trauma patients ($p<0.001$ for each versus medical), and patients requiring mechanical ventilation ($p<0.001$).
CONCLUSIONS: ICU care results in substantial daily costs throughout the

course of the hospital stay. Pharmaceutical therapies with even nominal decreases in ICU LOS may significantly reduce total hospitalization costs.

188. The influence of drug copayment on antibiotic utilization in acute respiratory tract infections. *Muhammed S. Alsultan, Pharm.D.,* Ph.D., E. Paul Larrat, Ph.D.; University of Rhode Island, Kingston, RI.

PURPOSE: Many studies have demonstrated the inappropriate over-utilization of antibiotics in certain acute non-pneumonic respiratory tract infections (ARTIs). Factors behind this practice are many. Some have been studied and many still need more exploration. The objective of this study was to explore the effect of drug copayment on prescribing antibiotics in ARTIs. The study also estimated the potential savings, from the direct cost of drugs, to both the insurers and patients when paying for these medications that may be used inappropriately.
METHODS: A retrospective study of (n=1635) prescription events associated with different ARTIs was identified from the 1996 Medical Expenditure Panel Survey (MEPS). Descriptive analysis was used and a logistic regression model was conducted to evaluate the copayment effect on antibiotic utilization.
RESULTS: In 1996, the total spending on potentially inappropriate antibiotics for different ARTIs was around $394
million. The logistic regression analysis showed that drug copayments did not have a significant effect on the utilization of antibiotics in these conditions, with an odds ratio (OR) = 1.03 and a 95% confidence interval (CI) = 0.99 to 1.08 and a p-value of 0.1269.
CONCLUSIONS: The findings from this study provide more insight to insurer and designers of drug coverage plans, who should closely monitor prescribing patterns for ARTIs to avoid unnecessary cost as well as resistance from such antibiotics. However, more research is needed to examine the effect of the different copayment tier systems introduced in the last couple of years on the utilization of these medications.

189. Fondaparinux is cost-effective compared with enoxaparin as prophylaxis against venous thromboembolism in patients undergoing surgery for hip fracture. *Sean D. Sullivan, Ph.D.,* Susan R. Kahn, M.D., M.Sc., FRCPC, James E. Muntz, M.D.; University of Washington, Seattle, WA; Sir Mortimer D. Davis Jewish General Hospital, Montreal, PQ, Canada; Baylor College of Medicine, Houston, TX.

PURPOSE: The incidence of venous thromboembolism (VTE) after surgery for hip fracture is as high as 20-25% in spite of thromboprophylaxis. A clinical trial of fondaparinux, a new, synthetic, selective Factor Xa inhibitor, found an 8.3% rate of VTE (52/626) compared with a 19.1% rate (119/624) with enoxaparin after hip fracture surgery (odds reduction 61.6%; p<0.001). A cost-effectiveness analysis was undertaken using a cohort simulation model from the perspective of the health care payer.
METHODS: The analysis was based upon 7 days of prophylaxis and used data from patients in the fondaparinux clinical trial, supplemented with estimates from the published literature. Outcome probabilities were computed for a cohort of US patients receiving either fondaparinux or enoxaparin after hip fracture surgery. Costs were obtained from US health care databases. The cost-effectiveness analysis took into account efficacy and safety outcomes. Time horizon of the analyses included hospital discharge, 30 and 90 days and 5 years after discharge.
RESULTS: Fondaparinux is estimated to prevent 23.2 thromboembolic events (per 1000 patients) at 3 months compared with enoxaparin (NNT = 43), while producing cost savings per patient in 2002 dollars of $25, $138, $181, and $269 at discharge, 1 month, 3 months and 5 years, respectively. Sensitivity analyses show that results are robust to variations in all key parameters.
CONCLUSIONS: Fondaparinux is cost-effective in comparison with enoxaparin in hip fracture surgery, with improved efficacy outcomes.

190. Fondaparinux is cost-effective compared with enoxaparin as prophylaxis against venous thromboembolism in patients undergoing surgery for hip replacement. *Sean D. Sullivan, Ph.D.,* Susan R. Kahn, M.D., M.Sc., FRCPC, James E. Muntz, M.D.; University of Washington, Seattle, WA; Sir Mortimer D. Davis Jewish General Hospital, Montreal, PQ, Canada; Baylor College of Medicine, Houston, TX.

PURPOSE: The incidence of venous thromboembolism (VTE) after surgery for hip replacement is as high as 15-20% in spite of thromboprophylaxis. Pooled results from two clinical trials of fondaparinux, a new, synthetic, selective Factor Xa inhibitor, found a 5.0% rate of VTE (85/1695) compared with an 8.8% rate (151/1716) with enoxaparin after hip replacement surgery (odds reduction 45.3%; p<0.001). A cost-effectiveness analysis was undertaken using a cohort simulation model from the perspective of the health care payer.
METHODS: The analysis was based upon 7 days of prophylaxis and used data from patients in the fondaparinux clinical trial, supplemented with estimates from the published literature. Outcome probabilities were computed for a cohort of U.S. patients receiving either fondaparinux or enoxaparin after total hip replacement. Costs were obtained from U.S. health care databases. The cost-effectiveness analysis took into account efficacy and safety outcomes. Time horizon of the analyses included hospital discharge, 30 and 90 days and 5 years after discharge.
RESULTS: Fondaparinux is estimated to prevent 11.6 thromboembolic events (per 1000 patients) at 3 months compared with enoxaparin (NNT = 86). Compared with enoxaparin, fondaparinux saves $52, $76, and $119 per patient at 1 month, 3 months and 5 years respectively, but costs $12 more at discharge. Computations are based on 2002 dollars. Sensitivity analyses show that results are robust to variations in all key parameters.
CONCLUSIONS: Fondaparinux is cost-effective compared with enoxaparin in hip replacement surgery, with improved efficacy outcomes.

191. Fondaparinux is cost-effective compared with enoxaparin as prophylaxis against venous thromboembolism in patients undergoing surgery for knee replacement. *Sean D. Sullivan, Ph.D.,* Susan R. Kahn, M.D., M.Sc., FRCPC, James E. Muntz, M.D.; University of Washington, Seattle, WA; Sir Mortimer D. Davis Jewish General Hospital, Montreal, PQ, Canada; Baylor College of Medicine, Houston, TX.

PURPOSE: The incidence of venous thromboembolism (VTE) after knee-replacement surgery is as high as 25-30% in spite of thromboprophylaxis. A clinical trial of fondaparinux, a new, synthetic, selective Factor Xa inhibitor, found a 12.5% rate of VTE (45/361) compared with a 27.8% rate (101/363) with enoxaparin after knee replacement surgery (odds reduction 63.1%; p<0.001). A cost-effectiveness analysis was undertaken using a cohort simulation model from the perspective of the health care payer.
METHODS: The analysis was based upon 7 days of prophylaxis and used data from patients in the fondaparinux clinical trial, supplemented with estimates from the published literature. Outcome probabilities were computed for a cohort of US patients receiving either fondaparinux or enoxaparin after knee replacement. Costs were obtained from US health care databases. The cost-effectiveness analysis took into account efficacy and safety outcomes. Time horizon of the analyses included hospital discharge, 30 and 90 days and 5 years after discharge.
RESULTS: Fondaparinux is estimated to prevent 17.8 thromboembolic events (per 1000 patients) at 3 months compared with enoxaparin (NNT = 56), while producing cost savings per patient in 2002 dollars of $35, $108, $125 and $252 at discharge, 1 month, 3 months and 5 years respectively. Sensitivity analyses show that results are robust to variations in all key parameters.
CONCLUSIONS: Fondaparinux is cost-effective compared with enoxaparin in knee replacement surgery, with improved efficacy outcomes.

192. Blood costs survey at institutions conducting coronary artery bypass graft surgery: implications for management of blood transfusion practices. *Diana Isom, R.Ph.,* Jennifer Maurer, R.Ph., Ph.D.; Bayer Pharmaceuticals Corporation, West Haven, CT.

PURPOSE: Overall hospital costs range ~$26-33K per coronary artery bypass graft (CABG), and patients experiencing morbidity and mortality consume more hospital resources (cost per operative death, ~$74K; CABG w/return to surgery for bleeding, >$60K; added cost of perioperative stroke, ~$18K) across hospital cost centers. Blood transfusion in CABG is associated with costs and poorer outcomes such as stroke and death. Full-dose aprotinin (Trasylol; $1282 direct pharmacy cost) reduces blood loss and transfusion in primary
(% transfused: 54 placebo, 37 aprotinin; mean units: 1.7 placebo, 0.9 aprotinin) and repeat
(% transfused: 76 placebo, 47 aprotinin; mean units: 3.7 placebo, 1.6 aprotinin) CABG; full-dose aprotinin use in CABG reduces reoperations for bleeding and has been associated with a reduced incidence of stroke. The objective of the current study was to assess current US hospital costs of blood transfusion at institutions conducting CABG.
METHODS: A written survey was used to collect data from 5 US institutions' blood banks with active CABG programs (>400 CABGs/year) in 2001.
RESULTS: Mean overhead cost of administering transfusion (transport, blood bank service, typing, cross-matching) was $183. Additional unit costs varied by blood product and preparation methods (*phereses, leukoreduction, irradiation ± washing).

Blood Products	Means $/U	Ranges $/U
Fresh Whole Blood	147	130-164
Fresh Frozen Plasma	52	46-55
Platelet Concentrates*	95-111	47-159
Platelets*	457-493	375-610
Red Blood Cells*	125-217	104-225

CONCLUSIONS: These data confirm the significant costs associated with blood transfusion and indicate that immediate savings could be generated by reducing/eliminating transfusion. As costs and adverse outcomes could be avoided by decreasing blood transfusion, standard transfusion triggers and approved pharmacologic strategies such as aprotinin may be used to manage blood transfusion in CABG.

193E. Predictors of Health and Activity Limitation Index scores in individuals with self-reported irritable bowel syndrome (IBS) and IBS-like symptoms. *Patrick D. Meek, Pharm.D.,* Ismor Fischer, Ph.D., Sara S. Nibbe, Pharm.D.; University of Wisconsin at Madison, Madison, WI.

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194. Pharmacy audit of an evidence-based clinical practice guideline for the use of parenteral pantoprazole. Deborah B. Dunham, R.Ph., M.S., *Patrick D. Meek, Pharm.D.,* James M. Hoffman, Pharm.D., Mark Reichelderfer, M.D.; University of Wisconsin, Madison, WI.

PURPOSE: Pantoprazole injection was added to the University of Wisconsin Hospital and Clinics' [UWHC] medication formulary in February 2002. In order to define appropriate use, a set of guidelines were developed by the Section of Gastroenterology and the Department of Pharmacy. Zollinger Ellison syndrome, peptic ulcers (prior to endoscopy when there is evidence of significant bleeding) and gastrointestinal bleeding post-endoscopy (in patients who are at high risk for rebleeding) were defined as appropriate indications, and use for stress ulcer prophylaxis and NPO status were considered inappropriate indications. The purpose of this audit was to evaluate adherence to the UWHC guidelines for the use of intravenous (IV) pantoprazole.
METHODS: Data were collected from inpatients who received IV pantoprazole during a six-month timeframe (starting September 2002). A total of 61 patients received IV pantoprazole during the audit period. Medical records were obtained and reviewed for 40 of these patients (65.7%). The following data elements were collected: unit, service, attending physician, age, gender, date admitted, previous oral medication for acid suppression, indication for use, dose, and discharge acid-suppression medication.
RESULTS: Pantoprazole injection was used in both adult and pediatric patients, though only one (2.5%) patient was less than 18 years of age. Gastrointestinal bleeds were the most frequent indication for use of pantoprazole (42.5%), followed by stress ulcer prophylaxis (22.5%) and NPO status (20%). Fifty-five percent of patients received oral PPI and 7.5% received oral histamine$_2$ blocker therapy at the time of discharge.
CONCLUSIONS: Adherence to UWHC (indication and dosing) guidelines was low. Among patients treated with IV pantoprazole for indications other than GI bleeding, the largest subset was those receiving the drug for stress ulcer prophylaxis. The low adherence with the pantoprazole guidelines is particularly worrisome given the recent supply shortage.

195. Antiemetic therapy in postoperative nausea and vomiting: a cost-effective improvement initiative. *Eileen M. Sakai, Pharm.D.,* James A. Klauck, M.S., R.Ph., Cynthia R. Hennen, R.Ph., Amy W. Valley, Pharm.D.; Froedtert Memorial Lutheran Hospital, Milwaukee, WI; Pharmacy Healthcare Solutions, Grapevine, TX.

PURPOSE: To develop an algorithm for cost-effective management of postoperative nausea and vomiting (PONV) and evaluate impact on patient outcomes.
METHODS: A risk-stratification strategy and algorithm were adopted to estimate PONV risk and assign antiemetic therapy. Use of targeted drugs (ondansetron, dolasetron, and droperidol) was documented for surgical patients via retrospective chart review for February 2002 (Period 1) and compared to use during February 2003 (Period 2), 3 months post-algorithm implementation. The incidence of breakthrough PONV was estimated for inpatients by assessment of postoperative antiemetic use of targeted drugs.
RESULTS: A total of 704 (59% inpatient) and 783 patients (56% inpatient) received targeted drugs during Period 1 and Period 2, respectively. The number of orders for these 3 antiemetics was compared for the day of surgery, postoperative day #1 (POD #1), and postoperative day #2 (POD #2) for evaluation periods. The number of doses from Period 1 to Period 2 changed as follows: dolasetron 201 to 941 doses; ondansetron 1,154 to 9 doses; and droperidol 209 to 404 doses. The average individual doses of dolasetron and ondansetron also decreased. These trends resulted in annualized cost-savings of $128,044.80. For inpatients, the rates of breakthrough PONV decreased from 39.47% to 16.06% for day of surgery, 28.09% to 22.94% for POD #1, and 18.41% to 14.25% for POD #2 for Periods 1 and 2, respectively.
CONCLUSIONS: Implementing a pharmacy-driven antiemetic protocol for PONV resulted in a 46.32% ($128,044.80) reduction in annualized drug expenditures for prophylaxis and treatment of PONV, without compromising clinical outcomes.

Pharmacoepidemiology

196E. Clinical and economic outcomes in the thrombolytic treatment of peripheral vascular occlusion. *Alan F. Kaul, M.B.A, Pharm.D., FCCP,* Mandy C. Leonard, Pharm.D., BCPS, Kenneth Ouriel, M.D., T. Barry Katzen, M.D.; Medical Outcomes Management, Inc., Foxborough, MA; Cleveland Clinic Foundation, Cleveland, OH; Ohio State University, Columbus, OH; Baptist Hospital, Miami, FL.

Presented at the 28th Annual Scientific Meeting of the Society of Interventional Radiology, Salt Lake City, UT, March 27-April 1, 2003.

197. National and regional susceptibility of *Streptococcus pneumoniae* and Gram-negative isolates to third-generation cephalosporin antibiotics, 1994-2001: results of the Antimicrobial Resistance Management Program. *John G. Gums, Pharm.D.*; University of Florida, Gainesville, FL.

PURPOSE: This study determined national and regional susceptibility rates of *Streptococcus pneumoniae* and the gram-negative organisms *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* to third-generation cephalosporin antibiotics.
METHODS: The ongoing Antimicrobial Resistance Management (ARM) Program has collected more than 18 million isolates from 261 US institutions. Antibiograms and sensitivity reports of pneumococcal isolates for 1994-2001 were reviewed for susceptibility to cefotaxime and ceftriaxone; *E. coli*, *K. pneumoniae*, and *P. mirabilis* were reviewed for susceptibility to cefotaxime, ceftazidime, and ceftriaxone.
RESULTS: Nationally, from 1994-2001, *S. pneumoniae* isolate susceptibility was 75.6% to cefotaxime (n=9190) and 81.7% to ceftriaxone (n=25,481). Regionally, susceptibility was higher in the Northeast (85.1% cefotaxime; 90.6% ceftriaxone), South Central (80.7% cefotaxime; 86.0% ceftriaxone); and North Central (82.8% cefotaxime, 86.2% ceftriaxone) and lower in the Southeast (71.1% cefotaxime; 79.7% ceftriaxone). Nationally, *E. coli* susceptibility was 99.2% to cefotaxime (n=101,176), 97.8% to ceftazidime (n=160,493) and 99.3% to ceftriaxone (n=469,328). *K. pneumoniae* susceptibility was 98.0% to cefotaxime (n=31,304), 93.7% to ceftazidime (n=45,254), and 98.1% to ceftriaxone (n=143,214). *P. mirabilis* susceptibility was 99% to cefotaxime (n=17,384), 98.0% to ceftazidime (n=28,180) and 99.4% to ceftriaxone (n=81,795). Regionally, rates were similar for *E. coli*, *K. pneumoniae*, and *P. mirabilis*.
CONCLUSIONS: Nationally and regionally, *S. pneumoniae* isolates were more susceptible to ceftriaxone than cefotaxime, with sensitivity artificially suppressed, given that all isolates reflect breakpoints prior to January 2002, when NCCLS adopted a MIC ≥4 mg/ml for ceftriaxone and cefotaxime. Overall, gram-negative organisms had a high susceptibility rate to the third-generation cephalosporin antibiotics.

198. Vision, reading, and health literacy as predictors of medication adherence. *Michael D. Murray, Pharm.D., M.P.H.,* Jingwei Wu, M.S., Wanzhu Tu, Ph.D., Lisa Boggs, Daniel Clark, Ph.D., Michael Weiner, M.D., M.P.H., Dan Morrow, Ph.D.; Purdue University, Indianapolis, IN; Indiana University, Indianapolis, IN; Regenstrief Institute, Indianapolis, IN; University of Illinois, Champaign, IL.

PURPOSE: Ability to see, read, and comprehend written material would each seem to predict medication adherence. We conducted an interim study of whether vision, reading, and health literacy predict medication adherence in 109 older adults (≥ 50 years) with heart failure.
METHODS: Adherence was assessed as the percent of drug taken during six months to one year using electronic monitors. Vision was tested using the Snellen test (score range: 1 to 100). Ability to read was assessed using a previously validated instrument (range: 0 to 2). Health literacy was assessed using the Short Test of Functional Health Literacy in Adults (range: 0 to 36). Higher scores indicate better performance on all assessments. Because statistical testing was interim and considered exploratory, we set the level of significance at 0.1.
RESULTS: Patients were 64 ± 9 years of age, 69% female, 57% African-American, NYHA class distribution was I: 26%, II: 48%, III: 22%, IV: 4%. Mean adherence was 64% ± 29%, vision 59 ± 16, and reading 1.6 ± 0.6. Health literacy was 26 ± 11 with 68 % classified as having adequate health literacy. Univariate predictors of adherence included higher reading score (p=0.05), and higher health literacy score (p=0.03) or literacy level (adequate vs inadequate, p=0.01). In the multiple variable model controlling for demographic factors, either reading score (p=0.04) or health literacy score (p=0.09) were significant predictors.
CONCLUSIONS: Since the reading test is the quicker and easier assessment and could be conducted within a pharmacy, our preliminary conclusion is that it would be the most pragmatic predictor of adherence.

199. Magnitude of bias in studies based on cohorts of continuously enrolled subjects. *John Seeger, Pharm.D., Dr.PH.*; Ingenix, Auburndale, MA.

PURPOSE: Health insurance claims databases represent open cohorts: subjects are free to enter or leave and contribute variable follow-up time. Studies conducted within these databases sometimes limit subjects to those who are continuously enrolled over the study period in an effort to simplify analyses. This analysis sought to quantify the bias that can be observed in studies using this approach.
METHODS: Based on a hypothetical study of the effect of bisphosphonate therapy on the risk of hip fracture among persons with osteoporosis, this analysis used literature values for known associations and evaluated unknown associations over plausible ranges. Bisphosphonate efficacy (RRtrue) was evaluated across a range of estimates. The exposure-bias association is expressed as an odds ratio (EBOR), and the association between the bias variable and study outcome is expressed as a relative risk (RRbias). The potential spurious association between exposure and outcome is expressed as a relative risk (RRspurious), and was estimated using mathematical relations between RRbias and EBOR along with estimates of prevalence for exposure and bias variables.

RESULTS: This hypothetical study could produce a biased estimate of beneficial bisphosphonate effect (RRspurious=0.5) even under the assumption of no bisphosphonate effect (RRtrue=1.0). Under the assumption of bisphosphonate beneficial effect (RRtrue=0.6) such a study could produce an overestimate of effect (RRspurious=0.3). In sensitivity analyses, the bias (RRspurious) changed over the range of values evaluated.
CONCLUSIONS: Studies based on continuously enrolled subjects can suffer substantial bias in their effect measure. This analysis underscores the need for caution in the use and interpretation of studies employing this approach.

200. Use of a revised SHIM survey in minority men. *Stacy L. Martin, Pharm.D.,* Michelle G. Mattox, Pharm.D.; Carolinas Healthcare System, Charlotte, NC; Pfizer Inc., Charlotte, NC.

PURPOSE: The primary objective was to develop a revised Sexual Health Inventory for Men (SHIM) survey, determine ease-of-use and estimate prevalence of Erectile Dysfunction (ED) and associated risk factors in a minority population. Secondary objective was to determine if ED screening would identify patients with undiagnosed risk factors for ED.
METHODS: Four nurses in a minority clinic provided feedback on original SHIM regarding terminology that may be more easily understood by their patients. Consecutive men ≥ 40 years of age presenting to clinic over a 4 month period were asked to complete a revised SHIM. Nurses read the questions for illiterate patients, but offered no explanation. Data was collected on demographics, sexual functioning and known risk factors for ED; and analyzed using Microsoft ACCESS.
RESULTS: 194 men were offered the survey. 96% completed the survey. No patients asked for clarification of survey questions. 88% of patients completing the survey were African American, 8% Caucasian, 2% Hispanic and 1% Asian. Average age was 53.5, and average SHIM score was 15.6. SHIM score ≤ 21 was detected in 69.4% of men, indicating presence of signs and/or symptoms of ED. The most prevalent risk factor among men scoring ≤ 21 was hypertension (71%) followed by smoking (40%). Increasing age and number of risk factors were associated with declining average SHIM score. 8% of men with scores ≤ 21 had no documented risk factors and were referred for screening.
CONCLUSIONS: Revised SHIM survey was well accepted and easily completed. ED prevalence in this minority population was 69.4%, higher than the 52% reported elsewhere in a mostly Caucasian population. Utilizing this ED screening tool may help identify patients with undiagnosed risk factors for ED.

201E. Grouping drug-related problems for failure analysis. *Steven L. Clause, Pharm.D.,* Darren M. Triller, Pharm.D.; Albany College of Pharmacy, Albany, NY.

Presented at the 19th International Conference on Pharmacoepidemiology and the 1st International Conference on Risk Management, Philadelphia, PA, August 2003.

202. Prevalence of potential warfarin drug interactions: a retrospective study of outpatient prescriptions in Taiwan. *Mei-Shu Lin, R.Ph., M.S.,* Nen-Chung Chang, M.D., Ph.D., Yen-Hui Chen, Ph.D.; National Taiwan University; Taipei Medical University Hospital, Taipei, Taiwan.

PURPOSE: Drug interactions are a cause of warfarin-related problems. This study documented the potential drug-drug interactions in patients receiving warfarin at a teaching hospital in Taiwan to 1) estimate the prevalence of warfarin-related drug-drug interactions, and 2) examine the dosage of warfarin in drug-drug interactions and assess their clinical significance.
METHODS: Outpatient prescriptions between January 1 and December 31, 2001 at a teaching hospital in Taiwan were reviewed. Interacting drugs were selected from the warfarin monographs which clinical significance were classified as "1" in the 2002 Drug Interaction facts . The daily doses in the prescriptions were compared with Defined Daily Doses (DDDs), which is defined by World Health Organization.
RESULTS: Warfarin was prescribed in 17752 patient-time and 2915 patient-time (16.4%) of potential drug-drug interactions with clinical significance "1" was included. The most common of interacting drugs in our study is aspirin (1553/2915; 53.3%), the second is amiodarone (947/2915; 32.5%). The other interacting drugs include gemfibrozil, dextrothyroxine, quinidine, fenofibrate, and so on. The mean daily dose of warfarin in potential drug-drug interaction of our study is 2.5 mg.
CONCLUSIONS: Although our data suggest a relatively high prevalence of potential warfarin-related drug-drug interactions, the mean daily dose of warfarin is 2.5 mg, which is lower than 7.5 mg of defined daily dose. The further investigation is necessary to assess the clinical significance of warfarin-related drug-drug interactions at the mean dose of 2.5 mg. Furthermore, we urge clinicians and pharmacists to be alerted when prescribed or dispensed warfarin for patients.

Pharmacogenomics/Pharmacogenetics

203. Utility of clinic versus ambulatory blood pressure for pharmacogenetic studies. *Amber L. Beitelshees, Pharm.D.,* Issam Zineh, Pharm.D., Hossein N. Yarandi, Ph.D., Brian J. Puckett, Pharm.D., Taimour Y. Langaee, Ph.D., Daniel F. Pauly, M.D., Ph.D., Julie A. Johnson, Pharm.D.; University of Florida, Gainesville, FL.

PURPOSE: The current literature is inconsistent regarding the contribution of β_1-adrenergic receptor (β_1AR) genotypes to the antihypertensive effect of β-blockers. This inconsistency may be due to different methods for measuring BP. We hypothesized that ambulatory blood pressure monitoring (ABPM) would provide greater ability to detect the genetic contribution to β-blocker response than clinic blood pressure (CBP).
METHODS: Forty-seven untreated hypertensives were studied with ABPM at baseline and after titration of metoprolol. CBPs were recorded at each visit. All genotypes were determined by PCR and RFLP or Pyrosequencing. Response to metoprolol was compared by codon 389 genotype. Three types of multi-regression modeling (backward elimination, forward selection, and stepwise selection) were performed with a p-value <0.10 required for entry into the models. Variables included in the models were baseline DBP (DBP_B), age, sex, smoking status, BMI, exercise, race and β_1AR codon 49 and 389 genotypes.
RESULTS: DBP by ABPM was reduced by 11(±9)% in Arg389 homozygotes vs 5(±9)% in Gly389 carriers (p=0.04). Using CBP, DBP was reduced by 16(±7)% in Arg389 homozygotes vs 13(±8)% in Gly389 carriers (p=0.14). In addition, chi-square analysis was conducted to compare responders (defined as ≥10% reduction in DBP) and non-responders to metoprolol by β_1AR codon 389 genotype. A significant association was found only with ABP (68% Arg389 homozygote responders vs 46% Gly389 carrier responders,p=0.02) Each regression model using ABP included codon 389 genotype, whereas modeling with CBP did not include codon 389 genotype. Variables in the CBP models were DBP_B, codon 49 genotype, exercise, smoking status, and sex.
CONCLUSIONS: Response to metoprolol was significantly associated with β_1AR codon 389 genotype by ABP, but not by CBP. Our results highlight disparity using two different methods of measuring blood pressure and emphasize the importance of choosing appropriate methods for measuring phenotype in pharmacogenetic studies, especially with smaller sample sizes.

204. Impact of cytochrome P450 2D6 (CYP2D6) genotypes on metoprolol response rate and adverse effects among hypertensives. *Issam Zineh, Pharm.D.,* Amber L. Beitelshees, Pharm.D., Joseph R. Walker, Pharm.D., Brian J. Puckett, Pharm.D., Daniel F. Pauly, M.D., Ph.D., Michael S. Phillips, Ph.D., Craig A. Gelfand, Ph.D., Julie A. Johnson, Pharm.D.; University of Florida, Gainesville, FL; Orchid GeneShield, Princeton, NJ.

PURPOSE: We hypothesized that hypertensives with CYP2D6 genotypes causing the poor metabolizer phenotype would be most responsive to metoprolol and have higher adverse effect (AE) rates due to higher drug exposure.
METHODS: Hypertensive men and women underwent ambulatory BP monitoring (ABPM), then took metoprolol 50 mg BID with weekly titration to response, maximum dose, or intolerable side effects. ABPM was repeated after 4 weeks at stable dose. Patients were considered responders (R) to metoprolol if they had ≥ 10% reduction in daytime DBP from baseline. Steady-state S-metoprolol plasma concentrations (Cp) were measured, and area under the curve (AUC) was determined. AEs, recorded at weekly clinic visits, were classified as "dose-limiting" or "general" (defined as AE consistent with metoprolol pharmacology, likely to cause noncompliance, or a change in drug). AEs were assigned without knowledge of patients' genotypes. Genotypes were determined by PCR/single-base primer extension, with *2, *3, *4, *6, *9, *10, *17, *29, and *41 alleles used to classify patients as extensive, intermediate, or poor metabolizers (EM/IM, or PM).
RESULTS: ABPM and AE data were available on 36 and 52 patients, respectively (38 EMs, 10 IMs, and 4 PMs). There was a 47.2% response rate to metoprolol. 5.9% and 10.5% of R and non-responders (NR), respectively, were PMs. Mean AUC/dose was not different between R and NR, and EMs exhibited a 29.9-fold within-group variation in AUC/dose (mean ± SD, 3.19E-06 ± 2.38E-06 hour/ml). Dose-limiting and general AEs occurred in 13.5% (n=7) and 44.2% (n=23) of subjects, respectively. While no PMs experienced dose-limiting AEs, 75% experienced a general AE. 14.6% of patients with the EM/IM phenotype experienced a dose-limiting AE, and 41.7% experienced a general AE (p=NS for all comparisons).
CONCLUSIONS: In hypertensives, CYP2D6 genotype was not associated with response to metoprolol or rates of AE. There was a highly variable degree of drug exposure (AUC), even among patients with the same metabolizing phenotype. The impact of metabolizing enzyme gene polymorphisms on β-blocker response and tolerability should be investigated in other disease states in which β-blockers are used.

205. Plasma and whole blood histamine concentrations in healthy subjects with different histamine N-methyltransferase genotypes. *Yuen Yi Hon, Pharm.D.,* Michael W. Jann, Pharm.D.; Mercer University, Atlanta, GA.

PURPOSE: This study determined plasma and whole blood histamine concentrations in healthy subjects with different histamine N-Methyltransferase (HNMT) genotypes and assessed whether there are

differences in the concentration of plasma and whole blood histamine between HNMT homozygous wild type individuals and heterozygotes.
METHODS: A random blood sample was collected from unrelated healthy volunteers. HNMT C314T genetic polymorphism was determined by polymerase chain reaction – restriction fragment length polymorphism analysis. Plasma and whole blood histamine concentrations were determined by enzyme immunoassay kit. Mann-Whitney U test was used to compare plasma and whole blood histamine concentrations between HMMT homozygous wild type individuals and heterozygotes.
RESULTS: Thirty-five subjects (30 males, 5 females), age 21 to 40, participated in the study. Whereas 29 subjects (21 Caucasians, 2 African Americans, 2 Chinese, and 4 Indians) were found to be homozygous wild type, six Caucasians were found to be heterozygous mutant. Frequency of HNMT heterozygotes in this small Caucasian population was 0.22. The median plasma and whole blood histamine concentration for all subjects was 1.93 nM (1.03-7.24 nM) and 370 nM (27.4-919 nM), respectively. There were no differences (p=0.47) in the whole blood histamine concentration between HNMT homozygous wild type individuals (392 nM, 27.4-795 nM) (Median, Range) and heterozygous mutants (353 nM, 241-919 nM). Plasma histamine concentration appeared to be higher in HNMT heterozygotes (2.67 nM, 1.50-7.24 nM) than in homozygous wild type individuals (1.74 nM,1.03-6.39 nM) (p=0.14).
CONCLUSIONS: There was wide variability of plasma and whole blood histamine concentrations in healthy subjects. No differences were found in plasma and whole blood histamine concentrations between HNMT homozygous wild type individuals and the heterozygous mutants.

206. Aldosterone-mediated effects vary between rats with different angiotensinogen genotypes. *Larisa M. Humma, Pharm.D.,* Lucy F. Young, B.S., David L. Geenen, Ph.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: There are common genetic polymorphisms for angiotensinogen (AGT), a precursor hormone for aldosterone. The purpose of this study was to determine whether aldosterone-mediated effects on the kidney and heart vary by AGT genotype.
METHODS: Experiments were done in Brown Norway (BN) and Lewis rats, which have different restriction fragment length polymorphisms of the AGT gene. Twelve 4-month-old rats of each strain were fed a low (0.3%, n=6 of each strain) or high (8%, n=6 of each strain) sodium diet, to stimulate and suppress the renin-angiotensin-aldosterone system, respectively. After 2 weeks, rats were housed in metabolic cages for 24-hour urine collection. Urinary aldosterone, determined by radioimmunoassay, and sodium-to-potassium ratio (Na/K) were compared between strains. Six Lewis and 8 BN rats were maintained under standard conditions for 18 months, when harvested hearts were weighed and examined for collagen expression by Western blot.
RESULTS: With the high sodium diet, aldosterone secretion was suppressed, with < 25pg/ml per sample, and mean ± SD Na/K was similar between BN (5.2 ± 0.9) and Lewis (4.7 ± 1.6) rats. With sodium restriction, BN rats had greater mean ± SD aldosterone secretion (186 ± 39 vs 115 ± 33 mg/day, p<0.01) and lower urinary Na/K (0.07 ± 0.03 vs 0.42 ± 0.26, p=0.02) compared to Lewis rats. Consistent with these data, at 18 months, BN rats had a greater mean ± SD left ventricular weight-to-body weight ratio (202 ± 25 vs 147 ± 8 mg/100 g, p=<0.001) and collagen expression compared to Lewis rats.
CONCLUSIONS: These data suggest that AGT genotype may influence the quantity and physiologic effects of aldosterone, which in turn, could have implications for cardiovascular disease treatment strategies.

207. Pharmacogenomics and adverse drug reactions in cardiovascular drug therapy. *Stephanie S. Taber, Pharm.D.,* Lynda S. Welage, Pharm.D., FCCP, Michelle A. Leady, Pharm.D., Daniel S. Streetman, Pharm.D.; University of Michigan Health System; University of Michigan, Ann Arbor, MI.

PURPOSE: Genetic polymorphisms in transport proteins and drug-metabolizing enzymes may contribute to variability in medication response. This study evaluated the potential role of pharmacogenomics in cardiovascular (CV) medication-related adverse drug reactions (ADRs) at our institution over a four-year period.
METHODS: CV medication-related ADRs occurring between 1998-2002 were identified from a database that identifies ADRs using E-code analysis of discharge records. CV medications associated with the most ADRs were evaluated to determine the proportion with genetically-variable transport and/or metabolism. Both a random selection of all CV medications and of commonly-prescribed CV agents served as control groups. Differences in the proportion of drugs with genetically-variable transport and/or metabolism between groups were detected using chi-square analysis.
RESULTS: 12/31 (38.7%) of the drugs in the ADR group displayed genetic variation in transport and/or metabolism compared to 6/32 (23%) of those randomly selected from all CV medications and 14/39 (36%) of those from the commonly-prescribed CV medication group (p=0.14 and p=0.99, respectively). The three medications associated with the most ADRs (digoxin, warfarin, amiodarone) were all subject to genetically-variable transport and/or metabolism, and approximately 52% (248/480) of all ADRs involved at least one CV medication subject to genetic variability.
CONCLUSIONS: These results suggest that genetic variation in transport and/or metabolism may play a significant role in cardiovascular medication safety, as medications subject to variable transport and/or metabolism were over-represented among CV medications associated with ADRs. Prospective studies and further retrospective studies involving larger numbers of ADRs are needed to clarify the relationship between pharmacogenomics and ADRs.

208. Cytochrome P-450 mRNA expression in peripheral blood lymphocytes as a predictor of microsomal enzyme induction. *Curtis E. Haas, Pharm.D.,* Daniel Brazeau, Ph.D., Brent M. Booker, Pharm.D., Valerie Frerichs, Ph.D., Patrick F. Smith, Pharm.D., Thomas Kufel, M.D., Reginald F. Frye, Pharm.D., Ph.D.; University at Buffalo, Buffalo, NY; University of Pittsburgh, Pittsburgh, PA.

PURPOSE: To evaluate the potential for cytochrome P-450 (CYP) mRNA expression in peripheral blood lymphocytes (PBLs) to serve as an indirect measure of changes in CYP activity following enzyme induction.
METHODS: Twelve healthy volunteers were administered midazolam 0.025 mg/kg IV, omeprazole 40mg PO, caffeine 100 mg PO and debrisoquine 10 mg PO at 8 am on Day 1 and Day 9 of the study, and then blood samples and urine were collected for 8 hours. The subjects took rifampin 300 mg (n=6) or 600 mg (n=6) daily between the study days. Total RNA was isolated from PBLs on days 1 and 9. Plasma concentrations of midazolam, omeprazole and their primary metabolites were determined by LC/MS/MS, and plasma caffeine/paraxanthine and urinary debrisoquine/OH-debrisoquine by HPLC. CYP3A4 activity was estimated by midazolam clearance, CYP2C19 by the 2-hour omeprazole hydroxylation index (HI), CYP1A2 by the 8-hour caffeine metabolic ratio (CMR), and CYP2D6 by the urinary debrisoquine recovery ratio (DBRR). mRNA expression of the four CYP enzymes and GAPDH were determined by quantitative real-time PCR.
RESULTS: Midazolam clearance (0.38±0.09 vs 0.79±0.13; p=0.002), omeprazole HI (1.36±1.05 vs 0.39±0.32; p<0.001), and CMR (0.72±0.20 vs 0.97±0.32; p=0.007) all changed significantly following rifampin, consistent with enzyme induction. As expected, DBRR (0.38±0.28 vs 0.41±0.29) was not significantly affected by rifampin. CYP3A4, 1A2 and 2D6 mRNA content was measurable in all samples; CYP2C19 mRNA was inconsistently detectable. There were no systematic changes in the expression of the CYP mRNAs.
CONCLUSIONS: CYP mRNA expression in PBLs is not predictive of changes in enzyme activity following enzyme induction.

209. Assessment of sepsis in neonates using real-time quantitative polymerase chain reaction. *Thuy N. Nguyen, Pharm.D.,* Daniel A. Brazeau, Ph.D., Yvonne Brown, M.S., M.T., Peter Gal, Pharm.D., J. Laurence Ransom, M.D.; University at Buffalo, Buffalo, NY; Women's Hospital of Greensboro, Greensboro, NC; Greensboro Area Health Education Center, Greensboro, NC.

PURPOSE: To develop and evaluate a real-time quantitative polymerase chain reaction (PCR) methodology for the assessment of neonatal late-onset sepsis from blood samples in comparison with culture and procalcitonin (PCT) methods.
METHODS: Blood samples collected from 82 cases of suspected sepsis between August 2000 and April 2002 were divided into two groups: positive (n=50) and negative cultures (n=32). Universal PCR primers were chosen to amplify a portion of the 16S rRNA gene of eubacteria. DNA was isolated from 200 µmol of serum. Quantitative PCR was conducted for each sample using SYBR Green DNA staining to assess the concentration of the amplified products. In addition, human GAPDH was amplified as a normalization control. The 16S rRNA PCR product was cloned into a plasmid vector to build standard curves for absolute measurement of gene copy number. Procalcitonin serum levels were quantified using the immunoluminometric assay that detects two antigen-specific monoclonal antibodies bound to PCT.
RESULTS: The PCR yielded amplification products of the expected size for both 16S rRNA and human GAPDH. Real-time PCR detected sepsis levels over 6 orders of magnitude ranging from 0 to over 250,000 copies/sample. Median values of 16S rRNA copy number were at least an order of magnitude less for samples identified as negative by cultures and PCT methods.
CONCLUSIONS: Quantitative PCR was capable of detecting and quantifying sepsis in neonatal blood samples. The procedure is fast, less than 3 hours, and can be done with very small biological samples from a variety of sources.

Pharmacokinetics/Pharmacodynamics/ Pharmacometrics/Drug Metabolism

210. Aminoglycosides in intermittent hemodialysis: pharmacokinetic observations and treatment with a individualized dosing regimen. *William Dager, Pharm.D.,* Jeff King, Pharm.D.; University of California, Davis Medical Center, Sacramento, CA.

PURPOSE: To report observed aminoglycoside pharmacokinetic (PK) parameters and individualized dosing regimens in a consecutive series of acutely ill patients with renal failure requiring intermittent hemodialysis (HD).
METHODS: Patients receiving at least 2 days of aminoglycoside (AG) therapy

who required intermittent (HD), with at least one pharmacokinetic (PK) parameter calculable using levels drawn 12 hours or more after the initial dose. A PK Sub-analysis between end stage renal disease (ESRD) acute renal failure (ARF), prolonged treatment (>14 days) and potential influences of elimination during HD were done. Individualized regimens over 4 days were evaluated.
RESULTS: Records for 167 patients requiring HD receiving 250 courses of AG were evaluated. Mean Vd were 0.39 ± 0.15 (SD) L/kg (IBW), half-life ($t_{1/2}$) during IHD 4.2 ± 2.3 (SD) hours. The mean $t_{1/2}$ off IHD in ARF was 31.9 ± 20.8 (SD) hours and 45.7 ± 24.2 hours in ESRD. Mean ± SD peak levels measured 2 hours post infusion and pre-HD were 7.7 ± 1.6 and 3.9 ± 1.2 mg/L. The Vd, blood flow into the dialyzer and filtrate volume trended to correlate to AG HD $t_{1/2}$, but did not reach significance. Interdialytic $t_{1/2}$ progressively increased in subsequent weeks. The 117 treatment (non-synergy) courses in 100 patients receiving over 4 days of therapy had a 91% success rate.
CONCLUSIONS: Large variability in AG PK parameters with renal insufficiency requiring HD exists. Individualized regimens targeting peak levels of 7-10 mg/L and pre-HD levels of 3.5-5mg/L can achieve a high treatment success rate.

211E. Effects of amphetamine and methylphenidate on cytochrome P450 activity. *C. Lindsay DeVane, Pharm.D.,* Michael Pennick, B.S., Paul Hodgins, Ph.D., David A. Mays, Pharm.D., M.B.A., BCPS, Chris McDaniel, Ph.D., M. Alex Michaels, M.D., Simon J. Tulloch, M.D., Sherry L. Andes, Pharm.D.; Medical University of South Carolina, Charleston, SC; Shire Pharmaceutical Development, Inc., Rockville, MD; Shire US Inc., Newport, KY.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 19, 2003.

212. The effect of age on the pharmacokinetic of eplerenone. Susan E. Reid, M.Ed., Dwain S. Tolbert, Ph.D., James Ferry, Ph.D.; Pfizer Corporation, Skokie, IL; Takeda Pharmaceuticals, Lincolnshire, IL.

PURPOSE: Young or old, hypertension is a problem. Therefore, the effect of age on the pharmacokinetics of eplerenone, a selective aldosterone blocker (SAB) that reduces blood pressure, was evaluated in pediatric and adult patients with mild to moderate hypertension.
METHODS: This was an open-label, single-dose study conducted in 18 pediatric and 8 adult patients. Patients received 1 eplerenone tablet orally according to the patient's age as follows: 12.5 mg QD (2-5 years), 50 mg QD (6-11 years), 100 mg QD (12-16 years), 100 mg QD in adults (18-65 years). Blood samples were collected over a 24-hour period to characterize the single-dose pharmacokinetics of eplerenone.
RESULTS: Weight influenced the pharmacokinetics of eplerenone. Increases in weight were correlated to increases in the apparent central volume of distribution. No significant differences in the CL/F of eplerenone for pediatric hypertensive patients were observed when compared to adult hypertensive patients. When adjusted for body weight, there were no statistically significant differences between the adult and pediatric populations regarding dose-normalized overall exposure ($AUC_{0\text{-}24}$) or dose-normalized peak concentration (C_{max}) values for eplerenone; both AUC and C_{max} increased 15% (p=0.626) and 11% (p=0.568), respectively, for young patients (6-16 years) as compared to adult patients.
CONCLUSIONS: No statistically or clinically significant differences in eplerenone pharmacokinetics were observed between pediatric and adult patients. Single doses of eplerenone were well tolerated in both pediatric and adult hypertensive patients.

213E. A randomized, single dose study of bioequivalence of oxandrolone 10 mg tablets compared to oxandrolone 2.5 mg tablets. *Karin A. Greenberg, Pharm.D., BCPS,* Yih-Min W. Huang, Ph.D.; Bio-Technology General Corp., East Brunswick, NJ.

Presented at the Annual Meeting of the American Society of Health-System Pharmacists, San Diego, CA, May 31-June 4, 2003.

214E. Esopiclone: pharmacokinetic and pharmacodynamic effects of a novel anti-insomnia agent after daytime administration in healthy subjects. P. Leese, M.D., *Gary Maier, Ph.D.*; Quintiles Phase I Services, Lenexa, KS; Sepracor Inc., Marlborough, MA.

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215E. The sustained efficacy and safety of esopiclone over six months of nightly treatment: a placebo-controlled study in patients with chronic insomnia. Andrew Krystal, M.D., James Walsh, Ph.D., Thomas Roth, Ph.D., David A. Amato, Ph.D., Thomas Wessel, M.D., Ph.D.; Duke University Medical Center, Durham, NC; St. Luke's Hospital, Chesterfield, MO; Henry Ford Hospital, Detroit, MI; Sepracor Inc., Marlborough, MA.

Published in Sleep 2003;26:A310.

216E. Esopiclone, a novel, non-benzodiazepine, anti-insomnia agent: efficacy and safety in a model of transient insomnia. Russell P. Rosenberg, Ph.D., Andrew Jamieson, M.D., *Judy Caron, Ph.D.,* Thomas Roth, Ph.D.; Northside Hospital Sleep Medicine Institute, Atlanta, GA; Presbyterian Hospital of Dallas, Dallas, TX; Sepracor Inc., Marlborough, MA; Henry Ford Hospital, Detroit, MI.

Published in Sleep 2002;45:A68-69.

217E. Esopiclone, a novel, non-benzodiazepine, anti-insomnia agent: a six-week efficacy and safety study in adult patients with chronic insomnia. Gary K. Zammit, Ph.D., J. Christian Gillin, M.D., Louis McNabb, M.D., *Judy Caron, Ph.D.,* Tom Roth, Ph.D.; Sleep Disorders Institute, New York, NY; University of California, San Diego, CA; St. Jude Medical Center Sleep Disorders Institute, Fullerton, CA; Sepracor Inc., Marlborough, MA; Henry Ford Sleep Center, Detroit, MI.

Published in Sleep 2003;256:A297.

218E. Definitive evidence that aripiprazole is a D_2 and 5-HT_{1A} partial agonist. *Lyle Laird, Pharm.D., BCPP,* Robert D. McQuade, Ph.D., Shaun Jordan, Ph.D., Ruoyan Chen, B.S., Yoshihiro Tadori, B.S., Frank Yocca, Ph.D., Tetsuro Kikuchi, DVM; Bristol-Myers Squibb Company, Plainsboro, NJ; Bristol-Myers Squibb Company, Lawrenceville, NJ; Otsuka Maryland Research Institute, Rockville, MD; Otsuka America Pharmaceuticals, Rockville, MD; Otsuka Pharmaceutical Co, Ltd., Tokushima, Japan; Bristol-Myers Squibb Company, Wallingford, CT.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 2003.

219E. Renal and hepatitic impairment on the pharmacokinetics of aripiprazole. *William R. Clark, Pharm.D., BCPP,* Steven Bramer, Ph.D., Susan Shoaf, Ph.D., Daniel Salazar, Ph.D., Suresh Mallikaarjun, Ph.D.; Bristol-Myers Squibb Company, Princeton, NJ; Otsuka Maryland Research Institute, Rockville, MD.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 2003.

220. Impact of untreated depression on hospitalized patients with myocardial infarction. *John A. Dougherty, M.B.A., Pharm.D.,* Marni Williams, Pharm.D. candidate, Judy McManus, Pharm.D.; Florida Hospital, Orlando, FL; University of Florida, Gainesville, FL; Pfizer, Inc., Orlando, FL.

PURPOSE: Depression is an independent risk factor for myocardial infarction (MI) and cardiovascular mortality. Post-MI discharge protocols recommend cardiovascular medications (i.e. β-blockers and anti-platelet agents); however, few incorporate mental health evaluations. Limited studies describe the impact of undiagnosed or untreated depression in MI-hospitalized patients. Study objectives were to assess depression detection and treatment among MI patients and compare outcomes related to length of stay (LOS) and hospital costs.
METHODS: A retrospective, observational review was conducted on randomly selected MI-hospitalized patients. Primary outcomes included: admission and discharge diagnostic rates of depression, antidepressant usage, documented signs and symptoms of depression among undiagnosed patients, LOS, and hospital expenditures.
RESULTS: Charts were evaluated from 101 patients. The depression rate according to past medical history was 21.7% (n=22). Twelve (12%) patients had signs and symptoms of depression, without a diagnosis. Patients with depressive symptoms not receiving treatment had a 1.15 greater average LOS than patients without symptoms (6.90 vs 5.75 days). Average admission cost for untreated patients with depressive symptoms was $2,718 greater than those without symptoms or diagnoses ($27,475 vs $24,757). One patient with depression symptoms received a psychiatric referral. Four patients were newly diagnosed and started therapy after the MI. Average LOS among these patients was 19 days.
CONCLUSIONS: Undiagnosed or untreated depression can have a grave effect on MI stabilization and management. Clinicians should be aware of the association of mental health with cardiovascular outcomes (i.e. morbidity and mortality) and encourage mental health evaluations in hospital-based post-MI discharge protocols.

221E. Aripiprazole vs placebo in acute mania. *John Shepski, Pharm.D., BCPP,* Paul Keck, Jr., M.D., Anutosh R. Saha, Ph.D., Taro Iwamoto, Ph.D., Darlene N. Jody, Ph.D., Stavros Tourkodimitris, Ph.D., Donald G. Archibald, M.Phil., Ronald Marcus, M.D.; Bristol-Myers Squibb Company, Princeton, NJ; University of Cincinnati, Cincinnati, OH; Otsuka Maryland Research Institute, Rockville, MD; Otsuka Pharmaceuticals Co., Ltd., Tokyo, Japan; Bristol-Myers Squibb Company, Lawrenceville, NJ; Bristol-Myers Squibb Company, Wallingford, CT.

Presented at the Annual Meeting of the American Psychiatric Association, Philadelphia, PA, May 2002.

222. Antipsychotic monotherapy with olanzapine, risperidone, and

quetiapine in the treatment of schizophrenia. *Douglas Faries, Ph.D.,* Baojin Zhu, Ph.D., Qin Jiang, M.S., Haya Ascher-Svanum, Ph.D.; Eli Lilly and Company, Indianapolis, IN.

PURPOSE: To compare the use of antipsychotic monotherapy among patients treated for schizophrenia with olanzapine, risperidone, or quetiapine.
METHODS: Data were abstracted from medical records in a prospective study of schizophrenia patients treated at six U.S. sites between 7/1997 and 8/2002. Regression was used to compare patients who were initiated on olanzapine, risperidone, or quetiapine on (a) days of monotherapy (use of no antipsychotic medication other than the index medication) in the year after initiation, and (b) percentage of patients on monotherapy 90, 180, and 360 days after initiation. Covariates included sociodemographics, prior medication use, and prior length of monotherapy.
RESULTS: There were 291 olanzapine, 215 risperidone, and 106 quetiapine initiators. The average number of monotherapy days in the year after initiation was 135, 119, and 78, respectively. Pairwise comparisons were statistically significant for olanzapine vs risperidone (p=0.009) and olanzapine vs quetiapine (p=0.044) but not for risperidone vs quetiapine (p=0.740). Treatment differences were larger for patients who were not receiving any other antipsychotic upon initiation of the index antipsychotic as compared to patients who were. Compared with risperidone and quetiapine, a greater percentage of olanzapine-treated patients were on monotherapy at 90, 180, and 360 days after initiating treatment.
CONCLUSIONS: Significant differences in the duration and the prevalence of antipsychotic monotherapy were observed among patients treated for schizophrenia with olanzapine, risperidone, or quetiapine. Olanzapine-treated patients had the longest duration on monotherapy and the highest percentage of patients on monotherapy followed by risperidone and quetiapine-treated patients.

223E. Long-term olanzapine/fluoxetine use in major depressive disorder: final data. Sara A. Corya, M.D., Scott Andersen, M.S., Holland C. Detke, Ph.D., Luann E. Van Campen, Ph.D., Todd M. Sanger, Ph.D., *Ahmed Deldar, Ph.D.,* Douglas Williamson, MBChB, MRCPsych, Sanjay Dubé, M.D.; Lilly Research Laboratories, Indianapolis, IN; University of Pittsburgh, Pittsburgh, PA.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 17, 2003.

224. Retrospective analysis of risk factors in olanzapine clinical trials in elderly dementia patients. *Thomas A. Hardy, M.D.,* Vicki P. Hoffmann, Pharm.D., Jonna Ahl, Ph.D., Ilya Lipkovich, Ph.D.; Eli Lilly and Company, Indianapolis, IN.

INTRODUCTION: Diabetes has been temporally associated with the use of antipsychotics. The risk of diabetes in elderly patients with dementia who are receiving antipsychotic medication is unknown.
METHODS: The olanzapine dementia clinical trial database was surveyed for treatment-emergent diabetes (TED) in patients over 65 years of age (elderly). TED was defined as having two post baseline random glucose values ≥ 200 mg/dL, or initiation of anti-diabetic medication, or clinical diagnosis of diabetes. Risk factors evaluated: age, ethnicity, hypertension, baseline body mass index (BMI) ≥ 27, maximum baseline glucose ≥ 140 mg/dl.
RESULTS: Seven studies included elderly patients without preexisting diabetes (n=1461). There were 875 patients who received olanzapine, 243 received active comparator, and 343 received placebo. The mean treatment exposure was 130 days, 179 days, and 116 days, respectively. Patients with TED (n=40) had similar mean BMI and mean age as those patients without TED. Elevated baseline glucose correlated significantly with the development of TED. Number of risk factors, individual risk factors, and treatment were not predictive of TED. Rates of TED were similar across treatment groups.
CONCLUSIONS: Only baseline blood glucose levels were significantly correlated with TED. The risk of TED in elderly patients with dementia was not significantly different among treatment groups. Elderly dementia patients should be assessed for risk of diabetes before antipsychotic therapy is begun.

225E. Incidence of presumptive tardive dyskinesia in elderly patients treated with olanzapine or conventional antipsychotics. *Bruce J. Kinon, M.D.,* Virginia L. Stauffer, Pharm.D., Chris Kaiser, Ph.D., Sara Kollack-Walker, Ph.D.; Eli Lilly and Company, Indianapolis, IN.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003.

226E. Differential rate of weight gain present among patients treated with olanzapine. *Bruce J. Kinon, M.D.,* Matthew D. Rotelli, Ph.D., Christopher Kaiser, Ph.D., Sara Kollack-Walker, Ph.D.; Eli Lilly and Company, Indianapolis, IN.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, May 21, 2003.

227. Use of atypical antipsychotic medications in psychiatric and non-psychiatric outpatient clinical practice. Saeeduddin Ahmed, M.D., Debashis Ganguly, Ph.D., *David L. Van Brunt, Ph.D.*, Jennifer Schultz, Ph.D.; Eli Lilly and Company, Indianapolis, IN; Ingenix, Inc., Eden Prairie, MN.

PURPOSE: This study examined the use of atypical antipsychotic medications in psychiatric and non-psychiatric outpatient practice settings.
METHODS: A descriptive analysis was conducted of a pharmacy claims database of 23 health plans, for outpatient medical, pharmacy and enrollment data from January 1, 2000 to December 31, 2000. The first filled prescription for olanzapine, risperidone or quetiapine during the study period was defined as the index prescription. ICD-9 codes were used to identify indications and comorbidities, based on nearest diagnosis in the claims (within 60 days pre- and 10 days post-index date).
RESULTS: A total of 3,618 patients met enrollment criteria. Olanzapine, risperidone and quetiapine accounted for 35.13%, 48.26% and 16.61% of prescriptions respectively. Among prescribers, 67% were psychiatrists and 33% were non-psychiatrists. Approximately 70% of all patients had at least one mental disorder diagnosed during the study period. Looking at the nearest primary diagnosis, depressive and bipolar mood disorders were the most common psychiatric indications. "Back disorders" (4.1%) and "pain"(3.4%) were the most common non-psychiatric indications. Mean treatment days for olanzapine, risperidone and quetiapine were 129.03, 135.71 and 135.41 respectively. Only 6% of patients switched therapy from their index medications to a different antipsychotic. The most common concomitant drug classes were antidepressants, anticonvulsants and benzodiazepines
CONCLUSIONS: Atypical antipsychotic medications are used by a variety of medical practitioners to treat mental and physical conditions. Non-psychiatric clinicians account for a third of these prescriptions. Associated diagnosis and concomitant drug use suggest broad application of these medications in clinical practice.

228E. A multicenter, randomized, double-blind, placebo-controlled trial of extended-release carbamazepine capsules (Carbatrol®) monotherapy in patients with manic or mixed bipolar disorder. Richard H. Weisler, M.D., *Sherry L. Andes, Pharm.D., BS.Pharm.*; Duke University, Raleigh, NC; University of North Carolina, Chapel Hill, NC; Carbatrol Study Group, Rockville, MD; Shire US Inc., Newport, KY.

Presented at the Annual Meeting of the American Epilepsy Society, Seattle, WA, December 9, 2002.

229E. Open-label, 6-month evaluation of the safety and efficacy of extended-release carbamazepine capsules (Carbatrol®) in patients with manic or mixed bipolar disorder. Terence A. Ketter, M.D., *Sherry L. Andes, Pharm.D., BS.Pharm.*; Stanford University, Stanford, CA; Carbatrol Study Group, Rockville, MD; Shire US Inc., Newport, KY.

Presented at the Annual Meeting of the American Epilepsy Society, Seattle, WA, December 9, 2002.

230. Benefits of compliance with long-acting risperidone in schizophrenia. Natalie C. Edwards, M.S., *Marcia Rupnow, Ph.D.,* Chris L. Pashos, Ph.D., Ron J. Diamond, M.D., Marc F. Botteman, M.S.; Janssen Pharmaceutica Products, L.P., Titusville, NJ; ABT Associates Inc., Cambridge, MA; Mental Health of Dane County, Madison, WI; ABT Associates Inc., Bethesda, MD.

PURPOSE: Consistent medication administration associated with long-acting risperidone is expected to translate into significant improvements in clinical outcomes for people with schizophrenia. We used modeling techniques to project the benefits of this product in terms of relapse prevention.
METHODS: Published medical literature, unpublished databases, and a clinical expert panel were utilized to populate a decision tree model comparing long-acting risperidone, oral risperidone (RIS), olanzapine (OLA), and haloperidol decanoate (HAL-DEC). The model captured outcomes related to different levels of compliance. RESULTS: The proportion of patients predicted by the model to experience a relapse requiring hospitalization in one year were 66% HAL-DEC, 41% RIS and OLA, 26% long-acting risperidone, while the proportion of patients with an exacerbation not requiring hospitalization were 61% HAL-DEC, 37% RIS and OLA, 24% long-acting risperidone. The mean number of days of relapse requiring hospitalization per patient per year were predicted to be 31 HAL-DEC, 20 RIS and OLA, 12 long-acting risperidone, while the mean number of days of exacerbation not requiring hospitalization were 8 HAL-DEC, 5 RIS and OLA, 3 long-acting risperidone. CONCLUSIONS: Predictive modeling suggests that long-acting risperidone can potentially lead to substantially lower rates and fewer days of exacerbation and hospitalization compared to currently available treatments.

231. The effects of quetiapine (Seroquel) on food intake and body weight in mice. *Mark B. Cope, Ph.D.,* Tim R. Nagy, Ph.D., David B. Allison, Ph.D.; University of Alabama, Birmingham, AL.

PURPOSE: Quetiapine (QUE), like other atypical antipsychotic drugs, causes weight gain in humans; however, mechanisms are poorly understood and there are few experimental models to investigate this effect. This study tested the effect of QUE on food intake and body weight gain in female C57BL/6J

mice.
METHODS: Three groups of 84 day-old mice were dosed orally (via peanut butter) with placebo (n=20), QUE 30 mg/kg body weight (LD) (n=20), and QUE 60 mg/kg body weight (HD) (n=20). Animals were dosed twice daily, at 900 hours and 1500 hours (lights off at 1800 hours) for four weeks. Body weights were measured weekly and mice were monitored daily for signs of toxicity. Forty-eight hour food intake was measured at the beginning of each week of treatment. ANCOVA adjusting for baseline body weights was used to test for significant differences between groups. Post hoc analysis was performed with Fisher's least square difference test. The criterion for statistical significance was $p<0.05$ (2-tailed).
RESULTS: Weight was affected by drug, $p<0.01$. Post-hoc analysis revealed that the change in body weight between baseline and study completion was significantly greater in the LD group ($p<0.001$) and the HD group ($p<0.0001$) compared to the placebo group. Change in body weight between LD and HD groups was significantly different ($p<0.05$). HD-treated mice had increased food intake relative to controls during two of the four weeks.
CONCLUSIONS: These results suggest that QUE causes weight gain in female C57BL/6J mice, and that weight-gain is affected by dose within the range studied. Increased caloric intake may contribute to weight gain; however, other factors, including energy expenditure, need to be investigated to determine the complete underlying mechanism(s) causing QUE-induced weight gain.

232. Changes in liver function with long-term quetiapine use in a veteran population. *Philip D. Roland, Pharm.D.*; Central Arkansas Veteran's Healthcare System, Little Rock, AR.

PURPOSE: Manufacturer recommendations for use of quetiapine include monitoring of hepatic enzymes. Transaminase elevations were reported greater than 3 times the upper limits of normal during 3- to 6-week trials were at 6% for Quetiapine compared to 1% for placebo. This study examined changes in liver function for patients treated long-term with Quetiapine at Central Arkansas Veteran's Healthcare System.
METHODS: A report of all patients receiving quetiapine from January 1, 2002 through June 30, 2002 at the Central Arkansas Veteran's Healthcare System was obtained from the pharmacy services administration. Ninety-nine patients had received six consecutive 30-day supplies of Quetiapine. These 99 patient records were selected for retrospective chart review. The review period was December 1, 2001 through December 31, 2002.
RESULTS: Liver function tests were available on 22 patients for periods ranging from 1 to 345 days (M=110.48, SD=123). There were no significant changes in liver function during the review period, SGOT, $t(21)=0.851$, $p=0.404$ and SGPT, $t(21)=1.17$, $p=0.255$.
CONCLUSIONS: There were no significant changes in liver function during the review period. This was unexpected since the manufacturer reports transaminase elevations greater than 3 times the upper limits of normal during 3- to 6-week trials at 6% for Quetiapine compared to 1% for placebo. The manufacturer reports asymptomatic, transient and reversible elevations in serum transaminases (primarily ALT) during clinical trials.

233. AIMS evaluation with long-term quetiapine use in a veteran population. *Philip D. Roland, Pharm.D.*; Central Arkansas Veteran's Healthcare System, Little Rock, AR.

PURPOSE: Central Arkansas Veteran's Healthcare System requires a neuroleptic note and AIMS evaluation for patients taking antipsychotics. The possibility of developing TD must be discussed with the patient and entered into their medical record upon initiation of treatment and annually thereafter. An AIMS evaluation should also be completed at least every six months to assess symptom progression and/or development of TD. This study evaluated the documentation of these quality assurance indicators for patients treated long-term with Quetiapine at CAVHS.
METHODS: A report of all patients receiving quetiapine from January 1, 2002 through June 30, 2002 at the Central Arkansas Veteran's Healthcare System found ninety-nine patients had received six consecutive 30-day supplies of quetiapine. These 99 patient records were selected for retrospective chart review from December 1, 2001 through December 31, 2002.
RESULTS: An AIMS evaluation was performed on 62 patients (62.6%) and a neuroleptic note was documented for 62 patients (62.6%). AIMS scores ranged from 0 to 19 for total score (M=2.55, SD=4.00), 0 to 4 for mild (M=0.47, SD=0.91), 0 to 4 for moderate (M=0.22, SD=0.72) and 0 to 1 for severe (M=0.33, SD=0.27).
CONCLUSIONS: An AIMS evaluation was performed on 62 patients (62.6%) and a neuroleptic note was documented on 62 patients (62.6%) during the review period. Note: these were not necessarily the same 62 patients. The overall low mean score on the AIMS evaluation suggests TD is not a significant problem in the patients who are evaluated. Approximately 38% of patients being treated long-term with quetiapine had no AIMS evaluation or neuroleptic note documented in their records.

234E. Adderall® XR dosed once daily in adult patients with ADHD. Richard H. Weisler, M.D., Allan Chrisman, Timothy P. Wilens, M.D., M. Alex Michaels, M.D., Simon J. Tulloch, M.D., *David A. Mays, Pharm.D., M.B.A., BCPS*; Duke University, Durham, NC; University of North Carolina, Raleigh, NC; Duke University Medical Center, Durham, NC; Massachusetts General Hospital, Boston, MA; Harvard Medical School, Boston, MA; Shire Pharmaceutical Development Inc., Rockville, MD.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003

235E. Dose proportionality of 20, 40, and 60 mg Adderall® XR in adults. Simon J. Tulloch, M.D., Neil Frazer, M.D., James C. Kisicki, M.D., Susan Clausen, Ph.D., Kathy Yu, Yuxin Zhang, Ph.D., *David A. Mays, Pharm.D., M.B.A., BCPA*; Shire Pharmaceutical Development, Inc., Rockville, MD.

Presented at the 43rd Annual Meeting of the New Clinical Drug Evaluation Unit, Boca Raton, FL, May 26-30, 2003.

236. Relative rectal bioavailability of fluoxetine in normal volunteers. *Christian J. Teter, Pharm.D.,* Judy C. Chun, Kinh Luan Phan, M.D., Oliver G. Cameron, M.D., Ph.D., Sally K. Guthrie, Pharm.D.; University of Michigan, Ann Arbor, MI.

PURPOSE: Determine the rectal bioavailability of fluoxetine capsules relative to oral bioavailability. Determine the acceptability of the rectal route of fluoxetine capsule administration.
METHODS: Two-period, crossover design with 30-day washout between sessions. Twenty milligram fluoxetine capsules were administered to seven healthy, drug-free, nonsmoking volunteers by the oral and rectal routes on two separate occasions. Blood samples were collected at baseline, and 1, 2, 4, 6, 8, 10, 12, 24 hours, as well as 2, 3, 4, 5, 7, 14, 21, 28 days following drug administration. Serum concentrations of fluoxetine and norfluoxetine were determined using HPLC with ultraviolet detection. Relative rectal bioavailability (AUC_{PR}/AUC_{PO}) of fluoxetine, norfluoxetine, and total (fluoxetine + norfluoxetine) were calculated for each individual.
RESULTS: Six subjects completed both phases of the study. The results indicated that with six subjects we have 80%, 99%, and 99% power to detect the difference in mean fluoxetine, norfluoxetine, and total (fluoxetine + norfluoxetine) AUC, respectively, given the standard deviation at a 0.05 two-sided significance level. The relative bioavailability of rectally administered fluoxetine was 15% [fluoxetine (2-28%; 95% CI), norfluoxetine (9-21%; 95% CI), and total (fluoxetine + norfluoxetine) (8-22%; 95% CI)]. There were no complaints or adverse effects following fluoxetine administration by either route.
CONCLUSIONS: Plasma concentrations of fluoxetine and norfluoxetine following rectal administration of fluoxetine capsules may be sufficient for bridging strategies if the patient cannot take oral medications; especially if higher or more frequent dosing is used. Improved rectal formulations, such as a fluoxetine suppository, may increase fluoxetine rectal bioavailability.

237E. Long-term safety and efficacy of Adderall® XR in children with attention deficit hyperactivity disorder. Mark C. Chandler, M.D., Frank. A. Lopez, M.D., Joseph Biederman, M.D., *Michael Jones, Pharm.D., M.S.*; North Carolina Neuropsychiatry, Chapel Hill, NC; Children's Developmental Center, Maitland, FL; Massachusetts General Hospital, Boston, MA; Harvard Medical School, Boston, MA; Shire US Inc., Newport, KY.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003.

238E. Clinical improvement with long-acting risperidone in patients previously receiving oral olanzapine. Robert Jones, Robert Lasser, M.D., *Ed Crumbley,* Cynthia Bossie, Ph.D.; Janssen Pharmaceutica Products, L.P., Titusville, NJ; Janssen Pharmaceutica Products, L.P., McDonough, GA.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 19, 2003.

239E. Core symptom remission in patients with schizophrenia receiving long-acting risperidone. Robert Lasser, M.D., Stephen Rodriguez, *Ed Crumbley,* Cynthia Bossie, Ph.D., Georges Gharabawi, M.D.; Janssen Pharmaceutica Products, L.P., Titusville, NJ; Janssen Pharmaceutica Products, L.P., McDonough, GA.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003.

240E. Can stable patients with schizophrenia improve? The impact of partial compliance versus constant therapy. Courtney Lonchena, Robert Lasser, M.D., *Ed Crumbley,* Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Georges Gharabawi, M.D.; Janssen Pharmaceutica Products, L.P., McDonough, GA; Janssen Pharmaceutica Products, L.P., Titusville, NJ.

Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003.

241. Single-dose pharmacokinetic study of escitalopram in adolescents and adults. *Antonia Periclou, Ph.D.,* Niranjan Rao, Ph.D., Tyler Sherman, R.Ph., CCRA, Daniel Ventura, Ph.D., Wattanaporn Abramowitz, Ph.D.; Forest

Laboratories, New York, NY

PURPOSE: In adults, escitalopram demonstrates linear pharmacokinetics, and a half-life of 27-32 hours, consistent with once-daily dosing. The objectives of this study were to assess tolerability and compare the pharmacokinetics of escitalopram in adolescent and adult subjects.
METHODS: In this open label, single dose study, healthy adolescent (ages 12-17; n=12) and adult (ages 18-35; n=12) subjects received10 mg escitalopram, and blood samples were collected at regular intervals up to 168 hours after dosing. Plasma concentrations of S- and R-citalopram and their metabolites were measured for the determination of pharmacokinetic parameters, including maximum plasma concentration (C_{max}), time to maximum concentration (T_{max}), area under the curve (AUC) and terminal half-life ($T_{½}$).
RESULTS: Eleven adolescents and all 12 adults completed the study. There were no significant differences between adolescents and adults in AUC (exposure). Mean C_{max} was approximately 26% higher in adolescents than adults (13.10 ± 2.76 ng/ml versus 10.39 ± 1.92 ng/ml; p = 0.0621). T_{max} in adolescents was approximately 3 hours compared with 4.5 in adults (p=0.0249) and $T_{½}$ was approximately 19 hours in adolescents compared with approximately 29 hours in adults (p=0.0275). There were no significant differences between adolescents and adults in any S-demethylcitalopram pharmacokinetic parameters. No measurable conversion of escitalopram to R-citalopram was observed. The safety and tolerability in adolescent and adult subjects was comparable.
CONCLUSIONS: Systemic exposure of escitalopram following a single 10 mg escitalopram tablet was similar in adolescent and adult subjects and is consistent with once-daily dosing.

242E. Time of dosing and food effects on aripiprazole pharmacokinetics. *Diane Ammerman, Pharm.D., BCPP,* Suresh Mallikaarjun, Ph.D., Daniel Salazar, Ph.D., Steven L. Bramer, Ph.D., J. Xie, Ph.D., I.E. Weston, Ph.D.; Bristol-Myers Squibb Company, Pittsburgh, PA; Otsuka America Pharmaceuticals, Rockville, MD; Bristol-Myers Squibb Company, Wallingford, CT; Otsuka America Pharmaceuticals, Rockville, MD; MDS Pharma Services, Ontario, OR.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 2003.

243. Use of antipsychotics and new onset diabetes among central Texas veterans. *Jamie C. Barner, Ph.D.,* Jason Worchel, M.D., Min Yang, M.S.; Central Texas Veterans Health Care System; University of Texas, Austin, TX.

PURPOSE: To determine whether new onset diabetes differs: 1) between atypical and typical agents when using intent-to-treat methodology and accounting for switchers; and 2) among atypical agents.
METHODS: Data from the Central Texas Veterans Health Care System were extracted from September 1995-November 2002 for continuously enrolled adult patients who had no previous (6 months) antipsychotic use and no previous (1 year) history of diabetes. The following variables were extracted: antipsychotic and diabetes medications, diagnoses, lab values, and demographics. The following three analyses were conducted: 1) intent-to-treat; 2) atypical only users, typical only users, and switchers or concomitant users (both atypical and typical users); and 3) any atypical use (combined both atypical only users and switchers or concomitant users) and typical only users.
RESULTS: Among those who met the inclusion criteria (n=3916), the overall incidence of diabetes was 7 percent. Chi-square analyses revealed that there was no significant difference in new onset diabetes between typicals and atypicals (p=0.2907) using intent-to-treat methodology. The second and third analyses, which accounted for switching and concomitant use, also showed that there was no significant difference (p=0.5068, p=0.8688, respectively) in new onset diabetes and use of antipsychotic agents. Among the atypical agents (i.e., olanzapine, quetiapine, and risperidone), there was no significant difference (p=0.5463) in new onset diabetes.
CONCLUSIONS: In this study of central Texas veterans, new onset diabetes between atypical and typical users and among atypical users was not significantly different. This result remained consistent when using both intent-to-treat methodology and when accounting for switching or concomitant users.

244. Incidence of antidiabetic medication use following atypical antipsychotic use in a Texas Medicaid population. *Tina C. Lopez, Pharm.D., M.S.,* Karen L. Rascati, Ph.D., Veronica S. Young, Pharm.D., Leroy C. Knodel, Pharm.D., Robert L. Talbert, Pharm.D., FCCP, BCPS; University of Texas, San Antonio, TX; University of Texas, Austin, TX; University of Texas Health Science Center, San Antonio, TX.

PURPOSE: To differentiate the incidence of using antidiabetic therapy (ADT) following atypical or typical antipsychotic therapy.
METHODS: Subjects prescribed either a typical or atypical antipsychotic agent in 2000 were extracted from the Texas Medicaid Vendor Drug Program Database. Subjects were excluded if they had received an antipsychotic agent in 1999 or an antidiabetic medication any time prior to antipsychotic use. Subjects who started ADT were evaluated for use of concomitant medications associated with the metabolic syndrome or with causing diabetes. The individual atypical antipsychotics were evaluated for average dose prescribed and time-to-use of ADT.
RESULTS: The typical antipsychotic group (TAG) was significantly older by 3 years and comprised a higher percentage of African American individuals (26% versus 21%) than the atypical antipsychotic group (AAG). Both groups had similar proportions of subjects starting DT (29/809 (3.6%) TAG versus 186/4124 (4.5%) AAG) and similar time-to-use (222 ± 245 days versus 274 ± 180 days, respectively). The AAG was prescribed valproic acid more often than the TAG who began ADT. Olanzapine, quetiapine and risperidone demonstrate similar rates of starting ADT. Similarly, no differences in time-to-onset of ADT were noted among each drug. The olanzapine group who started ADT was prescribed a significantly higher dose compared to those who did not start ADT (10.6 ± 8.8 mg/day versus 8.4 ± 6.7 mg/day, respectively).
CONCLUSIONS: Typical antipsychotic and atypical antipsychotic users demonstrate similar rates of starting ADT. No differences in the use of ADT were seen among olanzapine, quetiapine, and risperidone users.

245E. Long-term safety and efficacy of once-daily Adderall® XR in adults with attention deficit hyperactivity disorder. Richard H. Weisler, M.D., Joseph Biederman, M.D., Allan Chrisman, Timothy P. Wilens, M.D., M. Alex Michaels, M.D., *Karen Nishihara, Pharm.D., Ph.D.,* Simon J. Tulloch, M.D.; University of North Carolina, Raleigh, NC; Massachusetts General Hospital, Boston, MA; Harvard Medical School, Boston, MA; Duke University Medical Center, Durham, NC; Shire Pharmaceutical Development Inc., Rockville, MD; Shire US Inc., Newport, KY.

PURPOSE: This 12-month, open-label extension study assessed the long-term safety, efficacy, and quality of life associated with use of Adderall® XR (20, 40, or 60 mg once daily) in 223 adults (≥ 18 years) with attention-deficit/hyperactivity disorder (ADHD).
METHODS: Patients met DMS-IV criteria for ADHD and had a history of ADHD before age 7; all patients rolled over from a randomized, double-blind, placebo-controlled, forced-dose titration study of once-daily Adderall XR. The intent-to-treat (ITT) population included 221 adults (mean age 39.8 years). Safety measurements were collected throughout the study. Primary efficacy was assessed using the 18-item ADHD Rating Scale (ADHD-RS) for adults.
RESULTS: Patients who previously received placebo had the largest improvement in ADHD-RS scores (mean change –11.9 from baseline to endpoint; P<0.001). Patients who received Adderall XR with interruption showed significant improvement from baseline to endpoint (mean change –7.6; p=0.041), as did those with no interruption (mean change –6.0; p<0.001). The most commonly reported adverse events were dry mouth (42% of patients), anorexia (30%), insomnia (25%), and headache (21%).
CONCLUSIONS: Results of this interim analysis suggest that Adderall XR 20, 40, or 60 mg once daily is safe for the long-term treatment of adult ADHD. All patients showed continued symptomatic improvement with no evidence of drug tolerance.
Presented at the 156th Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 21, 2003.

Pulmonary

246. Compatibility of inhaled admixtures of N-acetylcysteine with bronchodilators and osmolality changes during nebulization. Tzung-Yi Lee, M.S., Chi-Ming Chen, Ph.D., Chun-Nin Lee, M.D., *Hsiang-Yin Chen, M.S., Pharm.D.*; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: This study was to determine the compatibility of a nebulizer solution admixture containing NAC/fenoterol or NAC/ipratropium at room temperature. Factors attributing to side effects during nebulization like pH and osmolality were also determined.
METHODS: The admixture of a nebulizer solution with distilled water was served as a control solution for the evaluation of compatibility of NAC/fenoterol or NAC/ipratropium nebulizer solution admixture. Aliquots (400 uL) of each admixture were removed immediately upon admixing (t = 0) and at 1, 2, 3, 4, 5, 6, 7 hours after mixing and assayed by HPLC. The admixture was considered compatible if more than 90% of initial drug concentration was present as compared to the control solution. Osmolality was measured by sampling 100 uL from the filling cup at a 5-minute interval during nebulization and by freezing depression method.
RESULTS: Adding NAC to fenoterol or ipratropium raised pH from 3.20 to 7.90 and 3.74 to 7.95, respectively. After a 7-hour mixing, fenoterol decreased to 93.71% and NAC to 92.54% of initial concentration. Ipratropium had a mean loss of 7.39% and 10.91% after one- and two-hour admixing with NAC, respectively. Mixing fenoterol or ipratropium with NAC raised the initial osmolality away from iso-osmolality to 1400.67 ± 4.51 and 1413 ± 11.79 mosm/kg, respectively.
CONCLUSIONS: The admixture of NAC/fenoterol was compatible for at least 7 hours, but the admixture of NAC and ipratropium should be used within one hour. The hyper-osmolal NAC/fenoterol or NAC/ipratropium

nebulizer solution should be diluted with 0.45% NaCl to decrease the initial osmolality.

247E. Superior bronchodilator effects of tiotropium vs ipratropium bromide in chronic obstructive pulmonary disease over a 1-year clinical trial. *Steven Kesten, M.D.,* W. Vincken, M.D., Ph.D., J.A. Van Noord, M.D., Ph.D., A.P.M. Greefhorst, T. Bantje, L. Korducki, D. Moonen, M.D., P.J.G. Cornelissen, M.D.; The Belgian/Dutch Study Group, Brussels, Belgium; The Belgian/Dutch Study Group, Heerlen, The Netherlands; The Belgian/Dutch Study Group, Hengelo, The Netherlands; The Belgian/Dutch Study Group, Breda, The Netherlands; The Belgian/Dutch Study Group, Alkmaar, The Netherlands; Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT.

PURPOSE: Tiotropium (Spiriva®) is a new, once-daily, inhaled anticholinergic bronchodilator with kinetic subtype selectivity (for M_3 and M_1 vs M_2 receptors). Efficacy and safety were evaluated in two multicenter, randomized, double-blind, parallel-group ipratropium bromide-controlled studies in patients with stable COPD.
METHODS: A total of 535 patients received tiotropium 18 µg once daily as a dry powder via the HandiHaler® device (n=356; FEV_1 = 1.25L) or ipratropium bromide 40 µg QID (n=179; FEV_1 = 1.18L) for 52 weeks. Pulmonary Function Tests (PFTs) were measured prior to drug inhalation (approximately 24 hours after the previous dose [trough] and over 3 hours post-dosing [average]).
RESULTS:

	Change in FEV_1 (L) from baseline				Change in FVC (L) from baseline			
	Trough		Average		Trough		Average	
Day	Tiotropium	Ipratropium bromide	Tiotropium	Ipratropium bromide	Tiotropium	Ipratropium bromide	Tiotropium	Ipratropium bromide
1	–	–	0.20	0.20	–	–	0.44	0.43
8	0.14*	0.02	0.27*	0.20	0.32*	0.08	0.55**	0.45
50	0.13*	0.00	0.27*	0.19	0.30*	0.08	0.57**	0.48
92	0.14*	0.00	0.26*	0.18	0.34*	0.13	0.57**	0.48
182	0.13*	-0.03	0.26*	0.13	0.34*	0.07	0.55*	0.43
273	0.12*	-0.02	0.24*	0.15	0.30*	0.10	0.53**	0.44
364	0.12*	-0.03	0.23*	0.13	0.32*	0.11	0.50	0.42

All means adjusted for center and baseline mean. Common baseline mean: FEV_1 1.19L and FVC 2.62L; *p<0.01 vs ipratropium bromide **p<0.05 vs ipratropium bromide

CONCLUSIONS: Tiotropium demonstrated superiority vs ipratropium bromide in trough as well as average FEV_1 and FVC, which persisted throughout the 1-year study period without evidence of tolerance. These data support the use of tiotropium as first-line therapy for the long-term maintenance treatment of COPD.
Published in Eur Respir J 2000;16(Suppl 31):55s.

248E. Tiotropium improves lung function, dyspnea, and quality of life in patients with chronic obstructive pulmonary disease. *Steven Kesten, M.D.,* Richard Casaburi, Ph.D. M.D., Donald A. Mahler, M.D., Paul W. Jones, Ph.D., FRCP, Charles W. Serby, M.D., Shailendra S. Menjoge, Ph.D., Theodore J. Witek, Dr.Ph., the American Study Group; Harbor UCLA Medical Center, Torrance, CA; Dartmouth-Hitchcock Medical Center, Lebanon, NH; St. George's Hospital, London, United Kingdom; Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT.

PURPOSE: Tiotropium is a once-daily inhaled anticholinergic bronchodilator for the treatment of COPD, which has been shown to improve spirometry and symptoms. We report the results of a second large study conducted in the United States to confirm the previously noted benefits (AJRCCM 2000;161(3):A749).
METHODS: One-year, double-blind, randomized, multi-center, placebo-controlled trial of tiotropium 18 µg via HandiHaler® in subjects with stable COPD. Trough FEV_1 (FVC) was defined as the FEV_1 (FVC) approximately 24 hours after administration of study drug. Dyspnea was assessed by the BDI/TDI, and QoL was assessed by the St. George's Respiratory Questionnaire (SGRQ).
RESULTS: A total of 470 subjects participated (tiotropium [T] – 279, placebo [P] – 191). Mean baseline FEV_1 was 1.04L (39.2% predicted) (T) and 1.00L (37.7% predicted) (P). Mean trough FEV_1 response improved in the tiotropium group compared to placebo at Day 8 (0.12L [T] vs 0.00L [P], p<0.01). This improvement was maintained for the entire trial (at 1 year: 0.11L [T] vs 0.05L [P]). Mean trough FVC improved 0.25L for T at 1 year compared to a decline of 0.03L for P (p<0.01). The mean TDI Focal score improved by 1.15 units with T relative to P (0.86 [T] vs 0.29 [P]) at 1 year (p<0.01). The SGRQ Total score improved by 3.4 units with T relative to P (3.0 [T] vs 0.4 [P]) at 1 year (p<0.05). The SGRQ Impacts score improved by 3.7 units with T relative to P (3.1 [T] vs 0.6 [P]) at 1 year (p<0.05).
CONCLUSIONS: Tiotropium was effective in improving spirometry, dyspnea and QoL in patients with symptomatic COPD. Benefits over placebo were maintained throughout the 1-year trial. Tiotropium, a once-daily inhaled anticholinergic bronchodilator, has efficacy parameters suggesting a role as a first-line therapy for those with regular symptoms due to airflow limitation from COPD.
Published in Chest 2000;118(Suppl 4):134s-5s.

249E. Reduction in the incidence rate of chronic obstructive pulmonary disease exacerbations with tiotropium. Mitchell Friedman, M.D., Stephan Lanes, Ph.D., *Steven Kesten, M.D.*; Tulane University, New Orleans, LA; Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT.

PURPOSE: Exacerbations of COPD contribute to significant morbidity and health care resource utilization in patients with COPD. Tiotropium (TIO), a once daily inhaled anticholinergic with prolonged M_3-receptor antagonism, has been associated with a reduction in exacerbations in 1-year and in 6-month placebo (PBO)-controlled clinical trials.
METHODS: To conduct a more rigorous assessment of the expected incidence rates for COPD exacerbations according to subgroups, data from the 1-year and 6-month placebo-controlled studies were pooled. Incidence rates (IR) were computed as the number of patients experiencing an event divided by the patient-years at risk. For the analysis, person-time was accumulated from onset of treatment until 30 days after the last day of treatment. Patients contributed person-time to the denominator only as long as they were in the study receiving treatment and at risk of being identified with an exacerbation. Rate differences (RD) = IR (TIO) – IR (PBO). *P*-values were calculated to help assess the statistical reliability of each rate difference.
RESULTS:

	Tiotropium		Placebo			
	Patient-years	IR*	Patient-years	IR*	RD*	P
Total	679	61.1	483	84.51	-23.4	< 0.01
Men	381	61.1	254	83.9	-22.8	< 0.01
Women	161	60.9	114	85.9	-25.9	0.02
< 61 years	162	63.0	103	88.5	-25.5	0.02
61-70 years	237	63.4	159	85.7	-22.3	0.01
> 70 years	143	55.1	107	78.9	-23.8	0.03

*Per 100 patient-years

CONCLUSIONS: Tiotropium reduces the incidence of COPD exacerbations by approximately 22-26 cases per 100 patient-years. The magnitude of the reduction in the exacerbations is uniform over age and gender.
Presented at the International Conference of the American Thoracic Society, Seattle, WA, May 16-21, 2003.

250E. Superiority of patient performance with the HandiHaler® compared with the MDI four weeks after instruction. Ronald Dahl, Vibeke Backer, M.D., Birgit G. Ollgaard, Fronke Gerken, M.S., *Steven Kesten, M.D.*; University Hospital Aarhus, Aarhus, Denmark; Bispebjerg Hospital, Copenhagen, Denmark; Boehringer Ingelheim A/S, Copenhagen, Denmark; Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany; Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT.

Published in Eur Respir J 2002;20(Suppl 38):247s.

Rheumatology

251. Patient beliefs toward branded and generic medicines: evidence from a sample of osteoarthritis sufferers. *Jane Chang, M.P.H.,* Teresa L. Kauf, Ph.D., Shelby Reed, Ph.D., Joelle Friedman, M.P.A., Kevin Schulman, M.D.; Center for Clinical and Genetic Economics, Durham, NC.

PURPOSE: Patients' beliefs about medications may influence the demand for new medicines and responses to drug utilization mechanisms, such as tiered copays. We report on a survey of osteoarthritis (OA) patients' attitudes toward branded and generic drugs.
METHODS: An internet-based survey was administered to 4,346 patients with self-reported OA. Respondents were asked on a 5-point Likert scale with seven positively- or negatively-worded statements to indicate their agreement concerning branded and generic medications. Factors associated with brand preference were examined using multivariable regression.
RESULTS: Demographics: mean age 55.3 years, 70.9% female, 92.2% white, 49.7% employed. The proportion favoring brands varied by characteristic: 16.5%, brands "more effective"; 18.4%, brands "worth extra cost"; 22.8%, brands and generics "different"; 7.1%, generics have "more side effects"; and 10.7%, generics "less safe". Of the latter group, only 31.8% also felt brands have fewer side effects. 18.7% would choose brands over generics, and 11.3% felt generics weren't always cheaper. Most respondents (57.8%) did not attribute any advantage to BN, but 42.2% expressed a brand preference on at least one statement (excluding "generics always cheaper"), and 23.4% on two or more. Only 1.3% favored brands on all six statements. Responses to positively- and negatively-worded questions were similar. The number of statements favoring brands was related to higher income (p<0.0001), higher recent OA pain level (p>0.0001), and female gender (p=0.0006).
CONCLUSIONS: Nearly two in five respondents agreed with statements that BN were superior to G in at least 1 aspect. However, few consistently perceived brand advantages over generics.

252. Osteoarthritis patients' willingness to pay for pain reduction. *Jane Chang, M.P.H.,* Teresa L. Kauf, Ph.D., Shelby Reed, Ph.D., Joelle Friedman, M.P.A., Mohamed Omar, Ph.D., Kristijan Kahler, Ph.D., Kevin Schulman, M.D.; Center for Clinical and Genetic Economics, Durham, NC; Novartis Pharmaceuticals, East Hanover, NJ.

PURPOSE: We examined osteoarthritis (OA) patients' willingness to pay (WTP) for pain reduction as an indication of unmet medical needs.
METHODS: 4,346 patients with self-reported OA completed an internet-based survey and reported their maximum WTP out-of-pocket for a 1-month supply of a hypothetical new drug that could reduce their OA pain by 50%. We assessed purchase likelihood using a $50 reference price and generic availability.
RESULTS: Mean age was 55.4 years; 70.9% were female, 92.2% white. Median and mean WTP were $25.00 and $31.25. Among the 22.3% of patients with WTP ≥ $50, 76.2% were likely to buy the new drug and 17.3% were unsure. WTP for patients whose current medications were "not at all effective" versus "highly effective" was $36.68 vs $27.19 ($p<0.001$). In regression analysis, WTP was related to higher recent pain level ($p>0.0001$) and higher income ($p>0.0001$). When all patients were told a generic was available, 2.0% would buy the branded drug, 13.5% would ask the pharmacist's advice, 39.6% would buy the generic, and 37.3% said it depended on the price difference. Mean WTP among these groups was significantly different ($p<0.05$): $59.30, $43.28, $35.39, and $25.70, respectively.
CONCLUSIONS: This study indicates that most OA patients are willing to pay for a new drug to decrease their pain, suggesting an unmet need in this population.

253. The cyclooxygenase (COX)-2 specific inhibitor valdecoxib does not affect methotrexate pharmacokinetics. *David D. Hoelscher, M.D.,* Aziz Laurent, M.D., Jiang Qian, Ph.D., Michael Snabes, M.D.; PPD Development, Inc., Austin, TX; Pfizer Inc., Skokie, IL.

PURPOSE: To determine the effects of valdecoxib on the pharmacokinetic (PK) and toxicity profile of methotrexate (MTX).
METHODS: A single-blind, 2-period crossover study was conducted in 13 patients having rheumatoid arthritis (RA) for ≥6 months and receiving a stable oral dosage of MTX (5-20 mg/week) for ≥3 months. Patients received valdecoxib 10 mg BID (2x US FDA recommended dose) or placebo on Days 1-7, and MTX (5-20 mg/week) on Days 0, 7, and 14. Patients crossed over to the alternative treatment (valdecoxib or placebo) on Days 8-14. Plasma and urine MTX concentrations were determined using validated high-performance-liquid chromatography with mass spectrometry detection. A separate pooled analysis from two 12-week RA efficacy trials evaluated liver transaminase (ALT, AST) levels and absolute neutrophil counts (ANC) in patients receiving valdecoxib 10, 20, or 40 mg QD with MTX relative to placebo + MTX.
RESULTS: Coadministration of valdecoxib 10 mg BID with MTX resulted in no statistically or clinically significant effects on plasma exposure (AUC) and renal clearance of steady-state MTX compared with placebo (Table). Valdecoxib + MTX and placebo + MTX were equally well tolerated. In the 2 RA efficacy trials, there were no significant changes from baseline in ALT, AST, or ANC in patients taking valdecoxib + MTX, relative to placebo + MTX (data not shown).

Least Squares Means PK Parameter	MTX 5-20 mg/week + Valdecoxib 10 mg BID	MTX + Placebo	Valdecoxib/ Placebo Ratio	90% CI
C_{max} (ng/ml)*	29.5	30.0	0.99	0.91, 1.07
T_{max} (h)	1.2	1.7		
$AUC_{(0\text{-}24)}$ (hr•ng/ml)*	107	119	0.90	0.75, 1.08
$AUC_{(0\text{-}\infty)}$ (hr•ng/ml)*	103	105	0.98	0.93, 1.04
$Tt_{1/2}$ (h)	2.6	2.6	1.00	0.92, 1.09
$CL/F_{(plasma)}$ (L/h)	9.9	9.6	1.03	0.97, 1.09
$CL_{(renal)}$ (L/h)	7.7	8.3	0.93	0.77, 1.08
Urine $Ae_{0\text{-}24}$ (0-24 h) (mg)	0.78	0.84	0.90	0.80, 1.05

*Dose adjusted to 1 mg.

CONCLUSIONS: Administration of valdecoxib 10, 20, or 40 mg QD had no meaningful effect on the PK of a weekly dose of MTX (5-20mg) in patients with RA. Sponsored by Pfizer Inc. and Pharmacia Corporation.

Substance Abuse/Toxicology

254. Unexpected sources of glycol exposure. Jincy M. John, Pharm.D., *Susan C. Smolinske, Pharm.D., BCPS, DABAT,* John Wilson, Ph.D.; Children's Hospital of Michigan Regional Poison Control Center, Detroit, MI; William Beaumont Hospital, Royal Oak, MI.

BACKGROUND: Propylene glycol (PG) is a known cause of lactic acidosis.
CASE REPORT: A 17 month old girl was found playing with a container of chafing dish fuel, labeled to contain diethylene glycol (DG) 98.5%. The quantity ingested was unknown, but believed to be small. Initial labs were normal and the child was asymptomatic. A toxic alcohol panel revealed no ethylene glycol, but a PG level of 54 mg/dL. Labs at 3/10.5 hours later showed Na+ 140/141, K+ 4.5/4.5, Cl- 109/111 CO2- 17/22 and AG 14/8. Serum lactate at 10.5 hours was 3.8 mmol/L. Repeat PG level was zero. An assay developed for DG showed none in the original serum, high DG but no PG in the fuel product. The child received only activated charcoal (AC) and IV fluids and was discharged uneventfully, with normalization of the lactate level. Questioning of the parents revealed that the child had recently been using baby toothpaste that contained PG. They insisted that the child used normal amounts, and spit out after each use. It was also noted that the AC product contained 14% PG, with no other sources of PG identified.
METHODS: A survey of toothpastes was made, identifying those that contained fluoride, PG, or both, and the relative concentration of the latter.
RESULTS: Of 73 fluoridated products, 11% contained PG. Of those containing PG, 27% were specifically marketed for pediatric use. Of 3 non-fluoridated products, 100% contained PG. PG is a common humectant in toothpaste. We were surprised to find high amounts of PG in activated charcoal. These sources may result in hyperlactemia, creating confusion in the evaluation of suspected toxic alcohol ingestion.

255. Three-year results of an ongoing pharmacist-managed tobacco cessation program at a veteran's administration ambulatory care clinic. *Larry A. Dent, Pharm.D., BCPS*; University of Montana, Missoula, MT.

PURPOSE: This project documents the results of an ongoing pharmacist-managed tobacco cessation program at the Missoula VA Clinic from November 1999 to December 2002.
METHODS: Patients who participated in one or more sessions of a three-session course were surveyed by telephone regarding their tobacco-use status in June 2001, December 2001, June 2002, and December 2002. Patient medical records were reviewed to determine whether they had used bupropion, nicotine replacement therapy (NRT), bupropion and NRT, or quit "cold turkey". In June 2002 the transtheoretical model for change was incorporated into the behavioral component of the program.
RESULTS: Of the 77 patients who participated from November 1999 to June 2001, 57 were contacted. Of these, 21 (36.8%) were tobacco free; 15 (71.4% of quitters) had used bupropion. Of the 82 patients who had participated by December 2001, 77 were contacted with 22 (28.6%) being tobacco free; all 22 had used bupropion. Of the 93 patients who participated by June 2002, 87 were contacted, and 25 (29.8%) were tobacco free; 23 of these 25 (92%) had used bupropion. Of 123 patients participating by December 2002, 99 were contacted and 37 (37.4%) were tobacco free; 26 of these (70%) had used bupropion.
CONCLUSIONS: An ongoing pharmacist-managed tobacco cessation program is capable of producing results comparable or better than other similar bupropion/NRT programs.

Transplantation/Immunology

256E. Establishing a limited sampling strategy for cyclosporine (Neoral®) in pediatric renal transplant patients. Joanne Li, B.Sc., Chris Cameron, B.Sc., Dawn Strong, Pharm.D., David S. Lirenman, M.D., *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP*; University of British Columbia; Children's and Women's Health Centre of British Columbia, Vancouver, BC, Canada.

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257. A prospective, two-phase study of intravenous immunoglobulin in hypogammaglobulinemia: pharmacokinetic characterization and a dosing nomogram. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP,* Crystal Amos, B.Sc., David Pi, MBBS, M.B.A., R. Robert Schellenberg, M.D.; University of British Columbia; St. Paul's Hospital, Vancouver, BC, Canada.

Purpose: Despite widespread use and a worldwide shortage of intravenous immunoglobulin (IVIG), its pharmacokinetic parameters are not well-defined. This two-phase prospective study was conducted to characterize the pharmacokinetics of IVIG in patients with primary hypogammaglobulinemia, and to use this information to test the validity of a dosing nomogram. As a secondary objective, the effect of nomogram dosing on patient health outcomes was evaluated.
Methods: In phase I, pharmacokinetic parameters of IVIG (Gamimune N 5%) in 15 adult patients (on a dosage of 0.3 -0.4 g/kg every 3 to 4 weeks) were calculated by obtaining serial IgG concentrations (via rate nephelometry) pre-infusion and at 0.5h and 1,2,3 weeks (n=15) and 4 weeks (n=12) following a steady-state dose. In phase II, a study dose was determined according to a nomogram (derived from first-order pharmacokinetics) designed to target an IgG trough concentration of 7g/L. Pre-steady-state IgG trough levels were obtained from 16 blinded patients prior to the next 5 infusions of their new study dose, and a new steady-state IgG trough concentration was obtained prior to the 6th infusion. Patients also completed health-related questionnaires at each of these 6 visits.
Results: Pharmacokinetic parameters obtained in phase I are listed in the following table:

	C_{max} (g/L)	C_{min} (g/L)	k (h^{-1})	$t_{1/2}$ (h)	AUC (g*h/L)
Mean±SD	14.7 ± 2.0	8.0±2.2	0.00095 ± 0.00038	837.5 ± 297.6	6382.4 ± 1688.9

Five patients had trough concentrations (range of 4.8 to 6.9g/L) that were lower than the target trough concentration of 7g/L; 2 patients had trough concentrations of 7.2 and 7.4g/L, respectively; and the remaining 8 patients had higher trough concentrations (8.6 to 12.9g/L). In phase II, a statistically

significant relationship was found between predicted and actual IgG steady-state trough concentrations (r^2=0.656, p<0.05) and percentage of prediction error (8.7%) was relatively low. No significant differences were found between answers of health-related questionnaires between study visits (p<0.05).
Conclusions: IVIG pharmacokinetics in patients with hypogammaglobulinemia demonstrate wide interpatient variability. This study demonstrates the superiority of a dosing nomogram vs empiric dosing based on weight to target specific IgG trough concentrations. Further studies using IgG trough concentrations should define optimal IVIG dosing for patient well-being without overuse of this valuable resource.

258. Incidence, significance, and management of aspergillus infections in solid organ transplant recipients. *David J. Quan, Pharm.D.,* John Roberts, M.D.; University of California at San Francisco Medical Center; San Francisco, CA.

PURPOSE: To determine the incidence, significance and management of aspergillus infections in solid organ transplant recipients.
METHODS: Patients who received a transplant at UCSF Medical Center from 3/95 to 8/01
were evaluated. Microbiology results were searched for aspergillus cultures. Medical records were reviewed to determine therapy and outcome.
RESULTS: For the time period, there were 40 patients with a positive aspergillus culture. A total of 2207 transplants were performed (1584 kidney/kidney-pancreas and 623 liver). Infection was located in the lung in 19 of 20 (95%), brain in 3 of 20 (15%) and IV line in 1 of 20 (5%) patients. There were a total of 54 cultures positive for aspergillus sp. *Aspergillus fumigatus* was the most common pathogen, seen in 47 of 54 (87%) cultures. Four of 20 (20%) patients had a proven infection, 11 of 20 (55%) had a probable infection and 5/20 (25%) had a possible infection. Survival was 0%, 55% and 100% respectively. Thirteen patients received IV amphotericin B, 16 received inhaled amphotericin B, 13 received itraconazole, 4 received caspofungin and 7 received itraconazole plus IV amphotericin B. Survival was 46%, 56%, 50%, 50%, and 29% respectively. Eighteen of 20 patients received more than one antifungal agent.
CONCLUSIONS: The incidence of aspergillus infection in this transplant population is low. Patients with a proven tissue invasive infection have a worse outcome than those with a probable or possible infection. Despite the use of IV amphotericin B in the treatment of aspergillus infections, the survival rate is low.

259. Evaluation of the impact of an oral cytomegalovirus prophylaxis regimen in liver transplant recipients. *David J. Quan, Pharm.D.,* Jamie Hirata, Pharm.D.; University of California, San Francisco Medical Center; San Francisco, CA.

PURPOSE: The purpose of this study is to measure the incidence of cytomegalovirus (CMV) in the post-liver transplant population who received an all oral prophylaxis regimen compared to a regimen that consisted of 7 days of intravenous ganciclovir followed by an oral regimen.
METHODS: This is a retrospective study comparing a historical group of liver transplant recipients (n=95) who received 7 days of intravenous ganciclovir followed by an oral regimen to the study group (n=72) who received an all oral regimen. Donor and recipient CMV antibody status, prophylaxis regimen, immunosuppression regimen, and CMV antigen and culture results were documented.
RESULTS: The incidence of CMV infection was similar between the historical and control groups.

CMV infection	Historical 6 (6.3%)	Study 5 (6.9%)*
Donor+/Recipient-	3	1
Donor-/Recipient-	1	1
Donor+/Recipient+	2	2
Donor-/Recipient+	0	1

*p>0.05; CMV infection stratified by donor/recipient CMV Ab status

A potential cost savings of $16,000 to $40,000 per year can be realized by avoiding the use of 7 days of intravenous ganciclovir.
CONCLUSIONS: An all oral CMV prophylaxis regimen is as effective as a sequential regimen that consists of 7 days of intravenous ganciclovir followed by an oral regimen. Significant cost savings can be realized by utilizing an all oral CMV prophylaxis regimen.

260. P-glycoprotein as one pharmacogenomic predictor of tacrolimus pharmacokinetics and clinical outcomes in liver transplant recipients. *Christine M. Formea, Pharm.D.,* Tuan Luu, B.S., Abdulkareem Albekairy, Pharm.D., Valerie Greene, P.A., Shiro Fujita, M.D., William van der Werf, M.D., Alan Hemming, M.D., Richard Howard, M.D., Alan Reed, M.D., Janet L. Karlix, Pharm.D.; University of Florida, Gainesville, FL.

PURPOSE: Tacrolimus is a macrolide immunosuppressant used to prevent allograft rejection in organ transplantation. P-glycoprotein (P-gp) is an ATP-dependent efflux pump that may play a significant role alone or in combination with other genetic factors in drug absorption/disposition of xenobiotics including tacrolimus. A Pg-p genotype (CC) has been associated with decreased drug exposure. This study aimed to determine the individual pharmacogenomic impact of P-gp on tacrolimus dosing and clinical outcome in liver transplant recipients.
METHODS: Forty-eight liver transplant recipients were stratified based on genotype. Phenotypic data including tacrolimus doses and trough concentrations were collected for the first 10 days post-transplant. Genomic DNA was isolated from 10mg of human liver tissue with subsequent P-gp (C3435T) genotyping performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).
RESULTS: This study included 48 liver transplant recipients. There were 10 homozygous wild-type (CC), 7 homozygous variant (TT), and 31 heterozygous variant (CT). After 10 days post-transplant, the variant group (TT) had a lower tacrolimus dose requirement than the wild-type (CC) group. Calculated creatinine clearances declined in all three groups after 4 months of tacrolimus use.

Parameters	CC (n=10)	CT (n=31)	TT (n=7)
Average tacrolimus trough level (ng/dL)	10.9	11.4	10.0
Average tacrolimus dose (mg/kg/d)	0.050	0.051	0.042
Average baseline CrCl (ml/min)	101.3	105.8	86.3
Average Month 4 CrCl (ml/min)	65.5	68.3	50.8

CONCLUSIONS: Liver transplant patients expressing P-glycoprotein TT genotype may require lower tacrolimus doses to maintain therapeutic levels. P-glycoprotein alone or in combination with other genetic factors may be a useful predictor of tacrolimus dosing requirements.

261. Cytochrome P-450 3A5 as one pharmacogenomic predictor of tacrolimus pharmacokinetics and clinical outcomes in liver transplant recipients. *Christine M. Formea, Pharm.D.,* Tuan Luu, B.S., Abdulkareem Albekairy, Pharm.D., Valerie Greene, P.A., Taimour Langaee, Ph.D., Shiro Fujita, M.D., William van der Werf, M.D., Alan Hemming, M.D., Richard Howard, M.D., Alan Reed, M.D., Janet L. Karlix, Pharm.D.; University of Florida, Gainesville, FL.

PURPOSE: Tacrolimus is a macrolide immunosuppressant used to prevent allograft rejection in organ transplantation. Cytochrome P-450 3A5 is believed to contribute alone or in combination with other genetic factors to total drug metabolism of xenobiotics including tacrolimus. A single nucleotide polymorphism (SNP) in CYP3A5 (A22893G) results in reduced in vivo catalytic activity. This study aimed to determine the individual pharmacogenomic contribution of CYP3A5 on tacrolimus dosing and clinical outcome in liver transplant recipients.
METHODS: Forty-eight liver transplant recipients were stratified based on genotype. Phenotypic data including tacrolimus doses and trough concentrations were collected for the first 10 days post-transplant. RNA was isolated from 10mg of human liver tissue followed by reverse transcription into cDNA and subsequent CYP3A5*1 and CYP3A5*3 genotyping performed by nested polymerase chain reaction (PCR).
RESULTS: This study included 48 liver transplant recipients. There were 31 homozygous wild-type (*1/*1), 15 heterozygous variant (*1/*3), and 2 homozygous variant (*3/*3). After 10 days post-transplant, CYP3A5 expressors (*1/*1 and *1/*3) had a higher tacrolimus dose requirement compared to CYP3A5 non-expressors (*3/*3). Calculated creatinine clearances declined in both groups after 4 months of tacrolimus use.

Parameters	*1/*1 (n=31)	*1/*3 (n=15)	*3/*3 (n=2)
Average tacrolimus trough level (ng/dL)	10.9	12.5	5.9
Average tacrolimus dose (mg/kg/d)	0.054	0.041	0.030
Average baseline CrCl(ml/minute)	104.2	96.0	103.1
Average Month 4 CrCl(ml/minute)	67.5	65.7	22.4

CONCLUSIONS: Liver transplant recipients expressing CYP3A5*3/*3 may require lower tacrolimus doses to maintain therapeutic levels. CYP3A5*3/*3 alone or in combination with other SNPs may be a useful predictor of tacrolimus dosing requirements.

262E. Mycophenolate compared to sirolimus in liver transplant recipients to spare calcineurin inhibitors. *Gregory A. Smallwood, Pharm.D.,* Laurel Davis, R.N., Enrique Martinez, M.D., Andrei C. Stieber, M.D., Thomas G. Heffron, M.D.; Emory University Hospital Pharmacy; Emory University, Atlanta, GA.

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263. Outcomes of liver transplant recipients with hepatitis C receiving interferon/ribavirin treatments in an outpatient transplant clinic. *Gregory A. Smallwood, Pharm.D.,* Laurel Davis, R.N., Enrique Martinez, M.D., Andrei C. Stieber, M.D., Thomas G. Heffron, M.D.; Emory University Hospital Pharmacy; Emory University School of Medicine, Atlanta, GA.

BACKGROUND: Treatment of recurrent hepatitis C (HCV) following liver transplant (OLT) currently includes α-interferon with ribavirin.
PURPOSE: The aim of this study is to evaluate patients receiving treatment for HCV recurrence following OLT.

METHODS: All OLT patients with serum RNA positive for hepatitis C with histological evidence of recurrence began treatment in a protocol directed outpatient transplant clinic.
RESULTS: Of 67 patients, there was a complete viral clearance in only 14.9 % (10/67). Fifty-three (79.1%) patients had a biochemical response by month 3. At 3 months there was a decrease in ALT [161 (± 91) u/L vs 71.2 (± 130) u/L; p = 0.003], total bilirubin [1.6 (± 0.9) ng/dl vs 1.2 (± 0.5) mg; p = 0.05], viral load (2.5 X 10^6 vs 0.9 X 10^6, p = 0.02) and AST [146 (± 500) u/L vs 68 (± 103); p = 0.002). Of the remaining 57 patients, 40 (70.2 %) were taken off of treatment due to adverse events. The remaining patients were begun on a non-responder protocol of pegylated µ-interferon /ribavirin (n = 17). Four (23.5%) patients had viral clearance with 3 (17.6%) patients maintaining a sustained response. African-Americans had lower survival (p = 0.01) and patients receiving > 15mg/day of prednisone (p = 0.03) at week 6 following liver transplant.
CONCLUSIONS: Following OLT, treatment of recurrent HCV is less effective than reported response rates with a high number of treatment failures, drop outs, and low survival for African-Americans or patients with higher prednisone doses.

264. Relationship between immunosuppression and osteoporosis in an outpatient liver transplant clinic. *Gregory A. Smallwood, Pharm.D.,* Debra Burns, Pharm.D., Enrique Martinez, M.D., Andrei C. Stieber, M.D., Thomas G. Heffron, M.D.; Emory University Hospital Pharmacy; Emory University, Atlanta, GA.

PURPOSE: The aim of this study is to determine the relationship between immunosuppression, disease state and osteoporosis in an outpatient liver transplant clinic.
METHODS: All liver transplant recipients visiting an outpatient transplant clinic received bone density scanning with a dual energy X-ray absorptiometry (DEXA) device of the calcaneal bone after completing a questionnaire assessing risk and medications currently being used.
RESULTS: Of the 137 liver transplant (OLT) recipients completing questionnaires and receiving DEXA screening, patients with low bone density (n = 50) were older [56.6 (± 12.7) years. vs 50.2 (± 10.1) years.; p = 0.02] when compared to normal density patients (n = 87) and were predominately female (64.0% vs 35.6%; p = 0.01). Based on disease state, patients with cholestatic liver failure had lower bone calcaneal area [17.3 (± 1.3) cm^2 vs 18.9 (± 1.57) cm^2; p < 0.01]. Patients taking tacrolimus (n = 112) compared to cyclosporine (n=25) had a tendency towards fewer low bone densities [37.5 % (42/112) vs 56.0% (14/25); p = 0.08] while having more risk factors [3.1 (± 1.2) vs 2.1 (± 0.8); p = .001] and higher prednisone dosing [4.4 (± 5.9) mg/day vs 2.1 (± 3.8) mg/day; p = 0.026]. For patient weaned from prednisone, tacrolimus group were less likely to have low bone density (36.2% vs 68.8%; p = 0.02). Mycophenolate did not influence bone density or area measured.
CONCLUSIONS: Following liver transplantation, patients taking cyclosporine were more likely to have low bone density compared to tacrolimus.

265. Association of CYP3A5*3 polymorphism with cyclosporine pharmacokinetics in healthy volunteers. *David I. Min, Pharm.D., FCCP,* Vicki Ellingrod, Pharm.D., BCPP, Howard McLeod, Pharm.D.; University of Iowa, Iowa City, IA; Washington University, St. Louis, MO.

Cyclosporine(CsA) is a substrate for CYP3A4, CYP3A5 and MDR1 gene product, p-glycoprotein and its pharmacokinetics is influenced by various factors including these genotypes. Recently, genetic variabilities of CYP3A5 have been reported in various ethnic groups.
PURPOSE: To determine the effect of CYP3A5*3 polymorphism on CsA pharmacokinetics among healthy volunteers.
METHODS: The pharmacokinetic study of oral CsA was performed in 16 healthy subjects. Blood cyclosporine concentrations were measured by high performance liquid chromatography. Concentration versus time data were analyzed by non-compartmental method using WinNonLin, and the blood samples were genotyped for the CYP3A5*3 and CYP3A5*6 using the polymerase chain reaction and a restriction digest. Each CsA pharmacokinetic parameters were compared using one way ANOVA test and each pair was compared by student t test for the difference.
RESULTS: There were six homozygous C/C (wild type), six homozygous T/T (variant) and four heterozygous C/T genotypes for CYP3A5*3 in these 16 healthy volunteers. In the case of CYP3A5*6, there were twelve A/A genotypes(wild type), four heterozygous A/G genotypes and one was not determined. According to the genotypes of CYP3A5*3, the mean pharmacokinetic parameters (±SD) of oral cyclosporine are as follows.

	C/C (wild)	T/T (variant)	C/T	p-value
T_{max} (hour)	1.8 ± 0.3	1.9 ± 0.7	1.6 ± 0.3	0.7
C_{max} (ng/ml)	1690 ± 658	1113 ± 173	1466 ± 350	0.066
$T_{1/2}$ (hour)	6.3 ± 2.6	6.0 ± 1.3	8.2 ± 2.8	0.680
AUC (ng.hour/ml)	7055 ± 1234	4896 ± 895	5997 ± 1632	0.031*
CL/F (l/hour)	12.2 ± 2.1	16.2 ± 3.9	13.6 ± 4.6	0.06

CONCLUSIONS: The CYP3A5*3 polymorphism appears to influence AUC of oral CsA significantly in healthy subjects. Further study with larger sample size may be needed to confirm these results.

266E. OKT3 vs daclizumab for induction and azathioprine vs mycophenolate mofetil for achieving steroid-free maintenance immunosuppression in cardiac transplant recipients. *Scott A. Chapman, Pharm.D.,* Kristine L. Gilkerson, R.N., Nancy L. Siemers, R.N., Connie Rooney, Bruce R. Lindgren, Marc R. Pritzker, M.D., Maria Teresa Olivari, M.D.; Minneapolis Heart Institute/Abbott Northwestern Hospital; University of Minnesota, Minneapolis, MN.

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267. Retrospective analysis of anemia and associated cardiovascular and renal allograft complications post-primary renal transplant. *Derrick R. Van Beuge, Pharm.D.,* K. Troy Somerville, Pharm.D., Lonnie D. Smith, Pharm.D., Lisa M. McDevitt, Pharm.D., Jackie Corbett, FNP-C., John Holman, Ph.D., M.D., Fuad Shihab, M.D.; University of Utah Hospitals and Clinics, Salt Lake City, UT.

PURPOSE: Anemia prevalence in adults after renal transplant is not defined. Anemia can cause exacerbation of cardiovascular disease and/or renal ischemia. Cardiovascular disease is the leading cause of mortality after renal transplantation.
METHODS: Medical records were reviewed defining the prevalence of anemia among primary renal transplant recipients at our center. Recipients 18 years and older, transplanted between 1999 to 2001 were included. Data collected: patient demographics, previous epoetin alfa and ACE-inhibitor use, Hgb, Hct, SCr, allograft and cardiovascular adverse events within the first year after transplant. Anemia definition: Males Hgb < 13 g/dl, females Hgb < 12 g/dl.
RESULTS: The study population included 114 patients, 72/114 (63%) males. Median age of the study group was 46 years (range: 32-60). Most recipients received a transplant from a deceased donor (67/114, 59%). The prevalence of anemia was 76%, 88%, 41%, 31%, and 26% prior to transplant, day of discharge, 3, 6, and 12 months, respectively. Some patients were (52/114, 45%) receiving epoetin alfa prior to transplant which was continued in only a few patients (3/114, 2.6%). Neither the use of epoetin alfa nor ACE-inhibitors prior to transplant had predictive value on Hgb response after transplant. The mean SCr for anemic patients at 12 months was 1.7 mg/dl versus 1.3 mg/dl in non-anemic patients (p<0.001). Allograft (delayed graft function, acute rejection) and cardiovascular (cardiomyopathy, MI) adverse events were higher among anemic patients.
CONCLUSIONS: Anemia after renal transplant remains problematic and should be addressed due to the potential for severe adverse events.

268E. Prospective abbreviated area-under-the-concentration and C2 Neoral monitoring in renal transplantation. *Yi-Min Ku, M.S., Pharm.D.,* Julle A. Stoner, Ph.D., R. Brian Stevens, M.D., John P. Leone, M.D., Ph.D.; University of Nebraska Medical Center, Omaha, NE; Lifelink Transplant Institute, Tampa, FL.

Published in Transplantation 2003;suppl 5(3):216.

269E. Assessment of interleukin-2 and soluble interleukin-2 receptor during chronic immunosuppression in renal transplantation. *Kathleen M. Tornatore, Pharm.D.,* Robin DiFrancesco, M.B.A., Kristin Johnson, Pharm.D., Andrea Rubino, Pharm.D., Alan Forrest, Pharm.D. Rocco C. Venuto, M.D.; University at Buffalo; Erie County Medical Center, Buffalo, NY.

Presented at the American Transplant Congress, Washington DC, May 30-June 4, 2003.

270E. Corticosteroid avoidance ameliorates lymphocele formation and wound healing complications associated with sirolimus therapy. *Christin Rogers, Pharm.D.,* J. Wesley Alexander, M.D., Rita Alloway, Pharm.D., Robyn Boardman, Pharm.D., Jennifer Trofe, Pharm.D., Michael Hanaway, M.D., Joe Buell, M.D., Michael Cardi, M.D., Prabir Roy-Chaudhury, M.D., Ph.D., V. Ram Peddi, M.D., E. Steve Woodle, M.D.; University of Cincinnati, Cincinnati, OH.

Published in Am J Transplantation 2003;3(Supp 5),Abstract #1298.

271E. Cardiovascular risk alterations with early corticosteroid cessation under modern immunosuppression: objective assessment by Framingham analysis. *Christin Rogers, Pharm.D.,* Rita Alloway, Pharm.D., Robyn Boardman, Pharm.D., Jennifer Trofe, Pharm.D., Michael Hanaway, M.D., J. Wesley Alexander, M.D., V. Ram Peddi, M.D., Prabir Roy-Chaudhury, M.D., Ph.D., E. Steve Woodle, M.D.; University of Cincinnati, Cincinnati, OH.

Published in Am J Transplantion 2003;3(Suppl 5);Abstract #241.

272. Post-transplant diabetes mellitus and sirolimus. *Agnes Lo, Pharm.D.,* Benjamin N. Gross, B.S., M. Francesca Egidi, M.D., A. Osama Gaber, M.D.; University of Tennessee, Memphis, TN.

PURPOSE: This study examined the incidence and risk factors of posttransplant diabetes mellitus (PTDM) in de novo renal transplant

recipients receiving sirolimus (SIR).
METHODS: This is a retrospective review of 66 renal transplant recipients initiated with SIR in combination with either tacrolimus (FK506) (n=39) or mycophenolate mofetil (MMF) (n=27) between 11/01/2000 and 10/30/2002. PTDM is defined as fasting blood glucose (FBG) >120mg/dl on two separate occasions and required treatment.
RESULTS: After a mean follow-up of 1.5 years, 15/66 (23%) [10/39 (25%) SIR-FK506 and 5/27 (19%) SIR-MMF, p=0.49] developed PTDM. The mean time to PTDM was 123 (2 to 372) days posttransplant. Prior to PTDM, the FK506 trough levels were between 4.6 and 5.8ng/ml and the SIR trough levels were between 10 and 15ng/ml. The demographics of PTDM and non-PTDM patients were similar except for a higher pretransplant body mass index (BMI) in PTDM patients (29 vs 26, p=0.05). Thirty-three percent of PTDM patients had a positive family history of DM and 80% had at least one FBG >120mg/dL during the first week posttransplant. At time of PTDM, the mean C-peptide level was 4.95 (2.1 to 8.6) ng/ml and the mean HgA1C level was 6.4% (5.5 to 8.4%). Oral hypoglycemics were initiated in all patients. 3/15 subjects subsequently required insulin and 2/3 had follow-up C-peptide levels of <0.8ng/ml.
CONCLUSIONS: The incidence of PTDM with SIR as primary immunosuppressant is similar to those reported with FK506. The risk factor for PTDM included elevated C-peptide and $HgBA_{1C}$ levels pretransplant, BMI >25, positive family history, and elevated FBG during the first week posttransplant. The high C-peptide level suggests that insulin resistance may be central to developing PTDM.

273. Disparate effects of immunosuppressants on influenza vaccine response. *Mary S. Hayney, Pharm.D.,* Deborah L. Welter, B.S.N., Mary Francois, B.S.N., Ann Marie Reynolds, B.S.N., Robert B. Love, M.D.; University of Wisconsin, Madison, WI.

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, but the ability to mount an antibody response may be limited by medications that prevent B cell proliferation. We hypothesized that antiproliferative immunosuppressant agents such as mycophenolate mofetil (MMF) and sirolimus, would be associated lower influenza vaccine response rates.
METHODS: Lung transplant patients and healthy individuals were enrolled prior to influenza season. Each individual had blood drawn prior to receiving the 2002-03 influenza vaccine and four weeks later. Influenza antibody concentrations were measured by hemagglutination inhibition assay. Vaccine response rates (antibody concentration ≥ 40 hemagglutination units (HAU) and at least 4 fold increase in antibody concentration) were compared using chi square or Fisher's exact tests. In addition, the influence of specific immunosuppressants on vaccine response was compared.
RESULTS: Sixty-eight lung transplant patients and 35 healthy controls participated. The response rate for lung transplant patients was 29/68 (43%) and 22/35 (63%) for the healthy individuals (p<0.05; chi square). Among the lung transplant patients, MMF was associated with poorer influenza vaccine antibody response (≥ 40 HAU) while sirolimus was associated with better influenza antibody response compared to other immunosuppressants.

Drug	Response rates	Percent	p value
On MMF	28/45	62%	0.01
No MMF	21/23	91%	
On sirolimus	20/22	91%	<0.02
No sirolimus	29/46	63%	

CONCLUSIONS: Lung transplant patients had lower influenza vaccine response rates than healthy individuals. Influenza vaccine antibody response is influenced by concomitant administration of MMF or sirolimus. Future studies should measure protection from influenza infection conferred by immunization and alternative vaccination strategies.

Urology

274E. Vardenafil improved patient satisfaction with erection hardness, orgasmic function, and sexual experience in men with erectile dysfunction following nerve-sparing radical prostatectomy. Jean Guy Vezina, M.D., *Jay C. Lee, M.D.*, Ajay Nehra, M.D., Gerald Brock, M.D., Peter Pommerville, M.D., Monica Seger, M.D., Harin Padma-Nathan, M.D.; Urology Clinic of Berger, Berger, PQ, Canada; University of Calgary, Calgary, AB, Canada; University of Western Ontario, London, ON, Canada; CanMed Clinical Research, Inc., Victoria, BC, Canada; Bayer, Inc., Toronto, ON, Canada.

Published in J Urol 2003;169:245.

275E. Sustained efficacy and tolerability of vardenafil (Levitra®) over two years in men with erectile dysfunction. Christian Stief, M.D., *Jay C. Lee, M.D.*, Hartmut Porst, M.D., Inigo Saenz De Tejada, M.D., Ernst Ulbrich, M.D.; Medizinische Hochschule, Hannover, Germany; Calgary, AB, Canada; Fundación para la investigación y el desarrollo en andrología, Madrid, Spain; Bayer Vital GmbH, Leverkeusen, Germany.

Presented at the 2nd International Consultation on Erectile and Sexual Dysfunctions, Paris, France, June 29-30, 2003.

276E. Development and validation of the Treatment Satisfaction Scale for erectile dysfunction. Maria Kubin, *Dana Britt,* Dorothy Keininger, Elyse Trudeau, Pierre Sagnier, Axel Fugl-Meyer, Manfred Beneke; Bayer Pharmaceutical, Wuppertal, Germany; Bayer Healthcare, West Haven, CT; Mapi Values, Lyon, France; Bayer Plc, Stoke Court, United Kingdom; Uppsala University, Uppsala, Sweden; Bayer Vital GmbH, Leverkusen, Germany.

Presented at the 2nd International Consultation on Erectile and Sexual Dysfunctions, Paris, France, June 29-30, 2003.

277E. Vardenafil improves erectile function in African-American, Hispanic, and Caucasian men with erectile dysfunction. *James Bennett, M.D.,* Angelina Trujillo; Midtown Urology, Atlanta, GA; Bayer Healthcare, West Haven, CT.

Presented at the Annual Meeting of the National Medical Association, Philadelphia, PA, August 2-7, 2003.

278E. Reliable efficacy over time of vardenafil in men with erectile dysfunction: a retrospective analysis of two pivotal phase III studies. Francesco Montorsi, M.D., *Wayne J.G. Hellstrom, M.D.,* Luc Valiquette, M.D., Ian Eardley, M.D., Martin Homering, MSPH, Ph.D., Tiemo-Joerg Bandel, M.D.; University Vita Salute, San Raffaele, Milan; Tulane University Medical Center, New Orleans, LA; St. Luke's Hospital, Montreal, PQ, Canada; Pyrah Department of Urology, Leeds, United Kingdom; Bayer AG, Wuppertal, Germany.

Presented at the 2nd International Consultation on Erectile and Sexual Dysfunctions, Paris, France, June 29-30, 2003.

Women's Health

279. Pharmacokinetics of intravenous immunoglobulin in pregnancy. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP,* Amanda Lai, B.Sc., Edwina Houlihan, R.N., Mary D. Stephenson, M.D., FRCSC, M.Sc.; University of British Columbia; Children's and Women's Health Center of British Columbia, Vancouver, BC, Canada

PURPOSE: To characterize intravenous immunoglobulin (IVIG) pharmacokinetics before and during pregnancy in women with recurrent miscarriage. To date, no such pharmacokinetic data for IVIG exist for this patient population, despite IVIG's usage in obstetrics, its expense, and worldwide shortage.
METHODS: Seven women with recurrent miscarriage were enrolled into this pilot study. Three were part of an open-label pharmacokinetic study for treatment of the antiphospholipid antibody syndrome (APS) in pregnancy and 4 were part of a randomized placebo-controlled trial for idiopathic secondary recurrent miscarriage. Of these subjects, 5 received IVIG (Gamimune N 5%) and 2 received placebo (in an equivalent volume of normal saline). Following informed consent, subjects received IVIG 500-1000 mg/kg (or placebo) over a 3- to 6-hour period every 4 weeks for up to 6 cycles and if conception occurred, continued to receive infusions every 4 weeks until 18-20 weeks of gestation. Subjects underwent serial blood sampling pre-infusion and at 0.5h and 1,2,3, and 4 weeks following the 1st dose, and a dose during each of the 1st and 2nd trimesters of pregnancy (i.e., weeks 10 and 18, respectively). Serum concentrations of IgG were measured by rate nephelometry and traditional noncompartmental pharmacokinetic analysis was performed. One-way repeated measures analysis of variance (followed by Student-Newman-Keuls test) was used to determine statistical significance within groups, defined as p≤0.05.
RESULTS: Mean (± SD) age was 40 ± 10 year (IVIG) and 35 ± 3 year (placebo). Pharmacokinetic parameters (mean ± SD) were:

	IVIG (n=5)			Placebo (n=2)		
	C_{max} (g/L)	C_{min} (g/L)	$AUC_{0-\tau}$ (g•h/L)	C_{max} (g/L)	C_{min} (g/L)	$AUC_{0-\tau}$ (g•h/L)
Pre-pregnancy	26.6 ± 4.9	13.5 ± 1.9	12393 ± 1770	12.1 ± 1.0	11.2 ± 0.5	7240 ± 1188
1st trimester	33.6 ± 8.4	14.9 ± 2.5[a]	13057 ± 2978	13.3 ± 0.6	11.1 ± 0.3	8010 ± 141
2nd trimester	27.2 ± 5.0	13.1 ± 2.9[a]	11488 ± 2072	10.5 ± 0.2	10.1 ± 0.1	6761 ± 322

[a]p=0.05

Dosage (on a mg/kg basis) did not differ within the IVIG group between the 3 sampling periods; nor were AUC values significantly different before and during pregnancy. The roughly-estimated contributions of exogenously-administered IVIG to the total $AUC_{0-\tau}$ [calculated as mean $AUC_{0-\tau}$ (IVIG group) minus mean $AUC_{0-\tau}$ (placebo group)] were 5153 g•h/L (pre-pregnancy), 5047 g•h/L (1st trimester), and 4727 g•h/L (2nd trimester).
CONCLUSIONS: In our patient population of patients with recurrent miscarriage, pregnancy did not have a significant effect on exposure to the same mg/kg dosage of exogenously-administered IVIG. The estimated contribution of exogenous IVIG (i.e., ~5000 g•h/L) to the total $AUC_{0-\tau}$ was similar to, albeit slightly lower than, that contributed by endogenous IgG (i.e., ~7000 g•h/L). These preliminary data warrant further study in larger groups of patients.

280. Treatment of antiphospholipid antibody syndrome in pregnancy: a randomized pilot trial comparing dalteparin to unfractionated heparin. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP, FCSHP,* Edwina Houlihan, R.N., Penny J. Ballem, M.D., M.Sc., FRCPC, Mary D. Stephenson, M.D., FRCSC, M.Sc.; University of British Columbia; Children's and Women's Health Center of British Columbia, Vancouver, BC, Canada.

PURPOSE: Despite only limited published pregnancy data, low molecular weight heparins are being used increasingly because of their once-daily dosing and theoretical advantages over unfractionated heparin. This randomized pilot trial was designed to compare dalteparin to unfractionated heparin for treatment of antiphospholipid antibody syndrome in pregnancy.
METHODS: Thirty-one patients who were contemplating pregnancy were entered into the study, following written informed consent. Twenty-eight of the patients met the Sapporo diagnostic criteria for antiphospholipid antibody syndrome, based on a history of recurrent miscarriage or at least one unexplained fetal demise. Patients were randomized to receive either prophylactic dosing of dalteparin (Fragmin®, Pharmacia and Upjohn) or unfractionated heparin (Hepalean®, Organon), initially prescribed in the luteal phase of the menstrual cycle and continued for six weeks postpartum, according to the following empiric regimens:

	Dalteparin	Unfractionated heparin
Pre-pregnancy	2,500u SC q24h	5,000u SC q12h
First trimester	2,500u SC q24h	5,000u SC q12h
Second trimester	5,000u SC q24h	7,500u SC q12h
Third trimester	7,500u SC q24h	10,000u SC q12h

All patients received low dose acetylsalicylic acid, started prior to conception. The primary outcome was a successful pregnancy. The secondary outcome was maternal and fetal complications.
RESULTS: Fourteen patients received dalteparin and 14 received unfractionated heparin. One patient in each group did not conceive. The mean maternal age at documentation of the index pregnancy was 34 years in each group. The dalteparin patients had a successful pregnancy outcome in 9 of 13 pregnancies (69%, 95% CI, 39-91%), compared to 4 of 13 pregnancies (31%, 95% CI, 9-61%) in the unfractionated heparin group. Spinal or epidural anesthesia was used with 8 deliveries in the dalteparin group and one delivery in the unfractionated group; no complications occurred.
CONCLUSIONS: The results from this pilot project suggest that dalteparin may be an effective alternative to UFH for treatment of antiphospholipid antibody syndrome in pregnancy. A multi-centered randomized trial is needed to determine the benefit to risk ratio.

281. Evaluation of post-menopausal women receiving hormone replacement therapy before and after termination of the estrogen plus progestin trial of the Women's Health Initiative. *Megan B. Bestul, Pharm.D.,* Joseph J. Saseen, Pharm.D., BCPS, Laura Hansen, Pharm.D., BCPS, Marianne McCollum, Ph.D., BCPS; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: The estrogen plus progestin study of the Women's Health Initiative (WHI) was terminated prematurely because of an increased risk of breast cancer and coronary artery disease with hormone replacement therapy (HRT); results which were extensively publicized in professional and lay press. The primary objective of this study was to determine the potential impact of the WHI results on HRT discontinuation rates.
METHODS: University-based clinic patients were identified via ICD-9 codes for menopause. Similar to the WHI population, women aged 50-79 taking HRT were included; those with hysterectomies were excluded. Two time periods were defined (pre-WHI, 7/9/2001-1/9/2002 and post-WHI, 7/9/2002-1/9/2003). HRT discontinuation/persistence and demographic information were collected.
RESULTS: ICD-9 codes identified 301 women with 98 meeting study criteria. Seven were eligible for pre-WHI, 13 for post-WHI. 78 women eligible for both groups were randomly assigned to pre- or post-WHI groups yielding equal groups (n=49 per group). There were no significant demographic differences between groups. Time-to-event analysis demonstrated an increased probability of HRT discontinuation in the post-WHI versus pre-WHI (log-rank test, $p<0.05$). Additionally, a cohort of women taking HRT one year prior to WHI (n=85) were followed for 18 months. HRT discontinuation rates were 8% (7/85) during the 12 months prior to WHI (7/9/2001-7/9/2002) and 39% (31/78) during the six months following WHI, with 30% (24/78) discontinuing within 3 months.
CONCLUSIONS: These data suggest that increased HRT discontinuation was temporally associated with the release of the WHI results. This implies that highly publicized outcomes data demonstrating harm can rapidly influence pharmacotherapy.

282. Comparing the pharmacokinetics of misoprostol sublingual and buccal administration. Eric Schaff, M.D., *Robert DiCenzo, Pharm.D., BCPS,* Stephen Fielding, M.D.; University at Buffalo, Buffalo, NY; University of Rochester, Rochester, NY.

PURPOSE: The purpose of this study was to compare the pharmacokinetics of misoprostol sublingual (SL) and buccal (BC) in healthy subjects.
METHODS: Healthy female subjects were randomized to receive 800 µg of misoprostol SL and BC. Plasma samples were drawn before and 0.25, 0.5, 0.75, 1, 2, and 4 hours after a single dose of study drug. There was at least a 4-day washout period between doses. Misoprostol was assayed by HPLC the lower limit of detection was 0.05 ng/ml and the CV% at 0.15 ng/ml , 0.8 ng/ml, and 4 ng/ml was 8.8%, 7.1%, and 5.6%, respectively. Pharmacokinetic parameters were determined using noncompartmental analysis and study days were compared using the paired t-test on the parameters or their log transforms when appropriate.
RESULTS: The median (interquartile range [IR]) $AUC_{0-\infty}$ was 1.91 h•ng/ml (1.17-2.68) and 0.484 h•ng/ml (0.350-2.03) and the AUC_{0-4} was 1.60 h•ng/ml (1.10-2.37) and 0.380 h•ng/ml (0.223-1.47) for SL and BC, respectively (n=8). Median (IR) C_{max}, C_{min} and half-life were 1.14 ng/ml (0.817-2.06), 0.0904 ng/ml (0.0250-0.199), and 1.49 hours (0.928-2.42) for SL and 0.229 ng/ml (0.140-1.16), 0.0562 ng/ml (0.0250-0.156), and 2.28 hours (1.70-2.49) for BC, respectively. There was a trend towards a higher geometric mean $AUC_{0-\infty}$ ($p=0.0641$), AUC_{0-4} ($p=0.0595$), and C_{max} ($p=0.0853$) for the SL route.
CONCLUSIONS: Sublingual administration appears to result in higher plasma concentrations of misoprostol compared to buccal. Small sample size is the most likely reason for the inability to reach statistical significance.

CLINICAL PHARMACY FORUM

These abstracts describe the delivery, development, justification, or documentation of innovative clinical pharmacy services; they may be descriptive only and need not contain an evaluative component.

283. Impact of pharmacists' interventions on drug-related problems and medication costs during ward rounds. *Ian Y.J. Wee, B.Sc.,* Wendy S.T. Ang, B.Sc., Siew-Luang Lim, B.Sc., Wee-Heng Lim, B.Sc., Siew-Huey Liew, B.Pharm.; Changi General Hospital, Changi, Singapore.

PURPOSE: To evaluate the impact of medication interventions by pharmacists on clinical benefit and medication costs, and to characterize the nature of drug-related problems and identify areas where physician education by pharmacists could be helpful.
METHODS: Pharmacists participated in multidisciplinary ward rounds and performed medication chart reviews for 10 months. Pharmacist interventions to drug-related problems were raised to the care team and the interventions was evaluated for their clinical significance and impact on inpatient medications costs.
RESULTS: A total of 944 interventions involving 781 patients were made. Antibiotics (35.3%), cardiac drugs (12.2%) and gastrointestinal agents (6.6%) were the drugs most often requiring interventions. Almost half of all drug-related problems were prescribing errors by junior physicians. The most frequent drug-related problems were inappropriate dosage regimen (38.9%), improper drug selection (12.4%) and drug interactions (7.2%). Dosage clarifications/adjustments (43.5%), recommendations for discontinuation of a drug (15.1%) and recommendations to switch to a therapeutically equivalent drug (10.3%) were the most common types of interventions made. These interventions contributed to optimisation of therapy, prevention of adverse events, and prevention of drug incompatibilities (62.3%, 25.4%, and 12.5%, respectively). Interventions were well accepted by physicians (82.5%), resulting in total medication cost savings of S$26140 (approx. US$15000).
CONCLUSIONS: Pharmacist participation in ward rounds led to improvements in drug therapy and patient safety, prevention of adverse effects, and medication cost savings. Pharmacists are also well placed to further improve the drug knowledge of physicians by focusing on commonly used groups of drugs and by targeting junior physicians.

284. The impact of intermittently available heel ultrasonography screenings on osteoporosis treatment patterns in a family practice setting. Terita L. Looney, Pharm.D., Jason D. Ayres, M.D., Katherine C. Herndon, Pharm.D., BCPS, *Renee M. DeHart, Pharm.D., BCPS*; Medical Center East Family Practice Residency Program; Pfizer, Inc.; Samford University, Birmingham, AL.

PURPOSE: To determine the impact of pharmacist-managed intermittent heel ultrasonography screenings in a family practice setting. Primary outcomes were the number of: DEXA scans performed, women diagnosed with osteoporosis, and antiosteoporotic medications prescribed after the screenings.
METHODS: Screenings were performed at a residency clinic for one year. Women screened that met National Osteoporosis Foundation (NOF) criteria for testing were compared to an age and race-matched unscreened control group meeting NOF criteria seen during the same year. The primary outcome measures were then compared for the two groups and statistically analyzed. The number of DEXA scans performed the year prior to the screenings was also compared to the number performed during the intervention year.
RESULTS: Eighty-one total patients were screened; 44 met NOF criteria for testing and did not have known bone disease at study onset. Twenty-one in the intervention group (47%) received referral for DEXA scan whereas two in the control group (5%) were referred. Eighteen patients in the study population (90% of those referred; 41% of total) referred for DEXA scanning versus one patient in the control group (50% of those referred; 2.3% of total)

had the test performed. Antiosteoporotic therapy was prescribed in 55% of the intervention group and 16% of the control group. All of these achieved statistical significance ($p<0.05$). When compared to the year prior to the screenings, there was a 79% increase in the number of DEXA scans performed.
CONCLUSIONS: In a family practice setting, intermittent osteoporosis screenings are associated with a significantly greater number of patients completing diagnostic testing and receiving pharmacotherapy for osteoporosis.

285. Implementation of a pharmacist-managed lipid clinic in a rural nurse practitioner practice. *Miranda R. Andrus, Pharm.D., BCPS,* Amy R. Donaldson, Pharm.D., Katherine C. Herndon, Pharm.D., BCPS; Auburn University, Auburn, AL; Pfizer, Inc., Birmingham, AL.

PURPOSE: To assess the lipid management and outcomes of patients enrolled in the pilot program of a pharmacist-managed lipid clinic in rural Alabama.
METHODS: A prospective study was designed to measure outcomes of an intensive pharmacist-managed lipid clinic in a small rural nurse practitioner practice. Twenty-two patients were enrolled in the pilot program. Lipid profiles obtained during the initial patient assessment and six follow-up visits were documented to assess response to drug therapy and goal attainment. Pharmacist interventions and patient adherence issues were also documented.
RESULTS: The mean age of the patient population (59.1% male) was 54.8 ± 9.5 years. Medication assistance programs (MAPs) were utilized by 54.6% of patients. The pharmacist completed 21 interventions related to lipid-lowering therapy over 132 patient visits. Among patients with a calculable LDL value at both the initial and last follow-up visits (n=13), the mean LDL cholesterol decreased from 140.7 ± 32.8 mg/dL to 114.6 ± 41.3 mg/dL ($p=0.02$). The goal LDL cholesterol was achieved in three patients at the initial visit and 11 patients at the last follow-up visit ($p=0.01$). The LDL cholesterol goal was achieved during one or more follow-up visits in 16 patients (72.7%). Statin monotherapy was the most commonly prescribed therapy (68.2%). Non-adherence to lipid-lowering therapy was reported in nine patients during 17 visits. MAP use was documented in eight of the nine non-adherent patients.
CONCLUSIONS: A pharmacist-managed lipid clinic can improve the outcomes of patients receiving care in a rural nurse practitioner practice.

286. Documentation of pharmacists' interventions and associated cost-savings: a practical approach. *Timothy J. Sayles, Pharm.D.*; University Medical Center, Fresno, CA.

PURPOSE: At Community Medical Centers, a project was undertaken to document the number and types of interventions made by our clinical pharmacists in three acute-care settings: an academic teaching hospital and two non-profit private community hospitals.
METHODS: Using a locally developed data-collection tool loaded onto personal digital assistants (PDAs), clinical pharmacists recorded 3471 interventions with medical and nursing staff at our facilities over a six-month period. We were then faced with the need to quantify the effect of these interventions on patient outcomes. We identified a study conducted in a similar health care organization that employed expert-review and rigorous statistical methodology.
CONCLUSIONS: The positive impact of clinical pharmacy services on health and cost-related outcomes has been well documented. Several methods have been published that assess the impact of pharmaceutical care on a variety of outcomes. Many of these studies focus on a single disease-state or particular practice setting, while others examine direct savings in drug costs alone, ignoring the impact of these interventions on indirect costs. Still others examine rates of incidence of adverse events or medication errors, and do not discuss associated cost-savings, or report cost-results in scales or terms with little practical utility. This paper describes a practical approach to adapting an appropriate methodology for use with locally collected data to make a compelling case to Hospital Administrators for implementing or expanding clinical pharmacy services.
RESULTS: Utilizing this approach, we were able to document a cost-avoidance of $1.3 million for 2295 evaluable clinical interventions made over a six-month period in our hospitals.

287. An evaluation of the global application of evidence-based strategies within a pharmacist-managed cardiovascular risk reduction service. *Kari L. Olson, Pharm.D.,* Jon Rasmussen, Pharm.D., Brian G. Sandhoff, Pharm.D., John A. Merenich, M.D.; Kaiser Permanente of Colorado, Denver, CO.

PURPOSE: Published data indicate that effective secondary prevention strategies for patients with cardiovascular disease (CVD) are under-utilized. Kaiser Permanente of Colorado developed a clinical-pharmacist managed cardiovascular risk reduction service (CPCRS) to help ensure CVD patients receive appropriate secondary prevention interventions. The purpose of this study was to evaluate the impact of CPCRS on the use of secondary prevention interventions.
METHODS: A computer-generated list of patients with documented CVD, enrolled in the service between June 1, 1998 and October 1, 2002 and followed for a minimum of 6 months was obtained. The proportion of patients on aspirin, β-blocker one-year post-MI, ACEi, lipid-lowering agents, and who had met their LDL goal of < 100 mg/dl was determined.
RESULTS: A total of 8,014 patients (>90% of our CVD population) met the entry criteria. The average age was 69 ± 10.2 years, 70% were male, and the average duration of follow-up of 2.5 years . Aspirin, β-blockers, and ACEi were used in 96.5%, 97.6%, and 49% of the population, respectively. The majority of patients (97.3%) had been screened for LDL-c. A total of 72.8% of patients achieved LDL-c < 100 mg/dl (average LDL-c 89.3 ± 24.1 mg/dl). The majority of patients (76.4%) received therapy with statins alone, 7.8% received combination therapy, and 12.7% received no therapy.
CONCLUSIONS: The services provided by CPCRS resulted in a large cohort of patients with CVD receiving appropriate secondary prevention strategies over both the short-and long-term. Furthermore, the proportion of patients achieving LDL-c control was significantly higher than previous reports.

288E. Hypertension management clinic: an innovative multidisciplinary approach. *Denise Waddell, Pharm.D.,* Martha Salazar, Pharm.D., Lisa Sliter, Pharm.D.; Gainesville VA Medical Center, Gainesville, FL.

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289. Impact of a reminder system on pneumococcal vaccination rates in a family medicine residency clinic. *Jennifer W. Childress, Pharm.D.,* Stephanie L. Evans, Pharm.D., Julie A. Brousil, Pharm.D.; St. Louis College of Pharmacy; Family Medicine of St. Louis, St. Louis, MO.

PURPOSE: This study documented pneumococcal vaccination rates in adults with diabetes to 1) compare a family medicine clinic's vaccination rates with national goals from the Healthy People 2000 initiative, and 2) determine the impact of a pharmacist-initiated reminder system on vaccination rates in this high-risk population.
METHODS: Medical records of 354 adult patients with diabetes followed in a family medicine clinic between January 2001 and July 2002 were reviewed in November 2002. Patients' vaccination status, type of diabetes mellitus, age, race, and date of last appointment were documented. Reminder sheets were placed in all medical records without documentation of pneumococcal vaccination. Medical records were again reviewed six months following the initial review and placement of reminder sheets.
RESULTS: Documentation of pneumococcal vaccination was found in 46% of 354 charts reviewed compared to the national goal of 60% from 2000. A greater proportion of patients ≥ 65 years of age received the vaccine compared to patients < 65 years of age (61% vs 42%, $p=0.009$). African-American patients were more likely to have been vaccinated compared to Caucasian patients (54% vs 32%, $p=0.002$). Following placement of the reminder sheets, a greater vaccination rate was found (57% vs 46%, $p=0.005$).
CONCLUSIONS: Overall vaccination rates were lower than the national goal for 2000 pre- and post-intervention. A significant improvement in vaccination rates among patients with diabetes was observed following implementation of a reminder sheet although further strategies to improve vaccination rates need to be identified to meet or exceed national goals.

290. Assessment of diabetic care associated with collaborative practice agreements between clinical pharmacists and physicians. *Patrick J. Kiel,* Amie D. McCord, Pharm.D., BCPS, Terri L. Jackson, Ph.D., R.Ph.; Dreyer Medical Clinic; Midwestern University Chicago College of Pharmacy, Downers Grove, IL.

INTRODUCTION: Diabetes Mellitus is associated with significant morbidity and mortality. Research indicates that patients are not optimally managed in the primary care setting. An innovative clinical pharmacy service in diabetes disease management was developed and implemented in an effort to improve clinical outcomes for referred patients with diabetes.
METHODS: The diabetes disease management program consists of intensive education by nurses and dieticians as well as education, laboratory monitoring, and frequent follow-up with a clinical pharmacist. Diabetic patients are referred to the program by their physician. Within the program primary care physicians are given the option to enter into a collaborative practice agreement with the pharmacist. This agreement allows the pharmacist to initiate, discontinue or adjust medications used to treat diabetes and related comorbidities including hypertension and hyperlipidemia. This service has been in place for approximately 18 months. Currently eighteen physicians have entered into collaborative practice agreements and over 400 patients have been evaluated.
RESULTS/CONCLUSIONS: Clinical outcomes for patients enrolled in this program are currently being assessed.

291E. Assessing the efficacy of erythropoietic agents in treating chemotherapy-related anemia: hematopoietic response vs area under the hemoglobin change curve. *Mei-Sheng Duh, M.P.H., Sc.D.,* Simone Peart Boyce, Pierre-Yves Crémieux, Ph.D., James Fastenau, M.P.H., R.Ph., Catherine Tak Piech, M.D.; Analysis Group, Inc., Boston, MA; Ortho Biotech Products, L.P., Bridgewater, NJ.

Presented at the Annual Meeting of the American Society of Health-System Pharmacists, San Diego, CA, May 31-June 4, 2003.

292E. The effect of pharmacist counseling and follow up on patient

outcomes following hospital discharge. Jeffrey L. Schnipper, M.D., M.P.H., *Jennifer L. Kirwin, Pharm.D., BCPS,* Michael C. Cotugno, Pharm.D., Stephanie Wahlstrom, Pharm.D., Brandon A. Brown, Pharm.D., Emily Tarvin, Carolyn Zanfini, Christopher Roy, M.D., Leroi Hicks, M.D., Sylvia C. McKean, M.D.; Brigham and Women's Hospital; Northeastern University, Boston, MA.

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293E. Real-time drug dosing recommendations in patients with renal insufficiency. *Erkan Hassan, Pharm.D.,* Michael J. Breslow, M.D., Brian Rosenfeld, M.D.; VISICU, Baltimore, MD.

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294. Creation of the clinical "K" tech: Development of the clinical technician as a supportive role to clinical pharmacy services. *Tamara Z. Kozlowski, B.S., Pharm.D.,* Patricia E. Kokoski, B.S., Pharm.D., Lawrence P. Siegel, M.A.S., Pharm.D., Michael C. Ranke, B.S., Marcia Watkins, C.Ph.T., Lynn Leucking, Patricia Rogers, Jennifer Gaertner, A.A.; Carroll County General Hospital, Westminster, MD.

PURPOSE: Carroll County General Hospital is a 194-bed, rural community, non-teaching hospital located in Westminster, Maryland. The expansion of clinical pharmacy services and control of drug costs was desired by the Pharmacy Department. The Clinical Technician position was created in May 2002 as an adjunct to expand these services, since an increase in pharmacist FTE positions was not an option. This position also allowed technicians an opportunity to work in a non-traditional role.
METHODS: The Clinical Technician training program included learning how to read a medical record, medication administration records, nursing flow sheets, lab reports and physician progress notes. The Clinical Technician works 32 hours per week (Monday-Friday). Daily duties include screening patients for inclusion in the IV to oral switch program and the renal dose adjustment program, and calculation of resource savings from these interventions. Discrepancies between pharmacy and nursing documented allergies, height and weight documentation, and Fosamax® administration times are also evaluated. In addition, the Clinical Technician helps collect MUE data and places medication profiles for surgery patients in the Medical Chart to aid post-op medication reordering.
RESULTS: With the creation of the Clinical Technician position, we were able to implement the IV to oral switch and the renal dose adjustment programs, resulting in an annualized savings of $41,928. This position has allowed the technician to become more involved in patient care and experience positive feelings of increased responsibility and trust from the pharmacists.
CONCLUSIONS: The Clinical Technician is a useful adjunct to clinical pharmacy services.

295. Development of a PDA application for opioid equianalgesic conversions. *Suzanne Amato Nesbit, Pharm.D., BCPS,* Stuart Grossman, M.D.; Johns Hopkins Hospital, Baltimore, MD.

PURPOSE: The Hopkins Opioid Program (HOP) is a Palm® application designed to facilitate appropriate conversions from one opioid or route of administration to another. The first opioid conversion program in the Johns Hopkins Oncology Center was developed and implemented in 1984 and is still available on the information systems computers. The increasing use of personal digital assistants (PDAs) by physicians, nurses and pharmacists, as well as the success of earlier versions, prompted the development of this program.
METHODS: Horizon Ware, Inc., Rockville, MD, was selected through a competitive BID process to develop the HOP for use on PDAs utilizing the Palm operating system. The Hopkins Opioid Program uses standard conversion information published in the peer reviewed literature, the Physicians Desk Reference, and guidelines published by national organizations such as the National Comprehensive Cancer Network, American Pain Society, and the Agency for Health Care Policy Research. This program is designed to facilitate dose equivalency calculations and to provide cautionary notes regarding drug choices; information about dosage forms available in pharmacies, and references where more comprehensive information is available.
RESULTS: The application is available as a free download from the Cancer Center's Web site. Since its completion in October 2002, over 1200 health care practitioners worldwide have downloaded the application.
CONCLUSIONS: The HOP allows clinicians to perform opioid conversions and to select appropriate opioid doses and dosage forms in a convenient PDA application. Plans are to convert the program to a Windows CE and a desktop PC format.

296. The impact of targeted drug programs in a surgical intensive care unit. Sharon L. Wilson, Pharm.D., Rachel Bongior, Pharm.D.; University of Maryland, Baltimore, MD.

PURPOSE: This study was designed to document the impact of a clinical pharmacist initiated targeted drug program on cost of drug therapy management in a surgical intensive care unit (SICU).
METHODS: Therapeutic interventions documented by a clinical pharmacist four days per week were evaluated between June and December 2002. Direct cost savings and avoidance were estimated based on the median to average length of stay in a surgical intensive care unit (2 to 5.9 days). Therapeutic targets included renal dosing of medicines, IV to PO conversions, discontinuation of inappropriate labs / therapies, and omission of labs/drug therapies.
RESULTS: A total of 300 interventions were documented over the study period. These interventions resulted in an estimated cost savings of $2896.79 to $8545.44 for the renal dosing and IV to PO interventions. Eighty-five percent of the drugs requiring adjustment for renal insufficiency were antibiotics. A total estimated cost avoidance of $5614.78 to $16,563.60 was derived from discontinuing inappropriate labs and drugs. There were 123 omission interventions documented. Of the drug therapies omitted, 34% involved re-dosing of medicines based on pharmacokinetic results. Because of the subjectivity of cost associated with these interventions, no cost analysis was performed. Overall net cost savings and avoidance for all programs were $8511.54 to $25,109.04 during the study period.
CONCLUSIONS: Targeted intervention programs initiated by a clinical pharmacist can impact the cost of drug therapy management in an intensive care setting. Acute care pharmacists having to balance direct care activities with other duties can still impact the care of patients in a SICU by decreasing unnecessary costs associated with drug therapy management.

297. The role of clinical pharmacists in mass arsenic poisoning. *Heidi Smith, Pharm.D.,* Karen Simone, Pharm.D., DABAT; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: To portray the role of intensive care clinical (ICPharm) and toxicology clinical pharmacists (ToxPharm) in diagnosing, responding to and providing continuity of care for victims of mass poisoning.
METHODS: Sixteen patients were admitted to the hospital with profound nausea, vomiting, diarrhea and hypotension after ingesting tainted coffee served at a church function. Etiology was unclear. Seven were admitted to a tertiary care center due to worsening symptoms and hemodynamic instability despite aggressive fluid resuscitation. Patients were admitted to both floor and intensive care beds. Initially unknown diagnosis, multiple involved health care workers, and diffuse location within the hospital made continuity of care difficult. The ICPharm streamlined patient care by accepting the role of coordinator for physicians, nurses, laboratory and the Poison Center information for patients at that hospital. The ToxPharm provided diagnostic, poison and antidote information.
RESULTS: The clinical pharmacists significantly impacted patient care. Along with poison center staff, the ToxPharm provided diagnostic information and arranged for the availability of antidotes and information regarding arsenic poisoning and treatment to the ICPharm. The ICCPharm coordinated therapeutic regimens, participated in discussions with families, and served in the communication to the media. The ICPharm and ToxPharm ensured the availability of large amounts of unusual chelating agents in a timely fashion.
CONCLUSIONS: Clinical pharmacists are important coordinators of patient care in mass exposures to unusual toxins, guiding therapy, obtaining medications and providing valuable medical information. Emergency preparedness plans should include clinical pharmacists.

298. Developing and implementing rasburicase guidelines in a cancer center. *Chin Y. Liu, M.S., Pharm.D., BCOP,* Rosalyn P. Sims-McCallum, Pharm.D., Rami B. Ibrahim, Pharm.D., BCPS, BCOP, Susan Seen, Pharm.D., Charles A. Schiffer, M.D.; Detroit Medical Center; Karmanos Cancer Institute; Harper University Hospital, Detroit, MI.

PURPOSE: Tumor lysis syndrome is a well-documented oncologic emergency. Hydration, urinary alkalization, and allopurinol are the standard of care in the treatment and prevention of hyperuricemia. Rasburicase is a new alternative for the management of hyperuricemia in patients with hematologic malignancies. In view of potential overuse of this agent and its high cost impact on pharmacy budgets, guidelines need to be developed and implemented to ensure the appropriate use of this agent.
METHODS: Criteria for the appropriate use of rasburicase were developed, approved by the Hematology/Oncology Pharmacy and Therapeutic Subcommittee and implemented by the pharmacy department in March 2003. All medical and pharmacy staff were educated on the process for ordering rasburicase.
RESULTS: The guidelines limit rasburicase use to one dose, as opposed to the 5 doses recommended by the manufacturer, in cancer patients with hyperuricemia and bulky tumor who require immediate chemotherapy. The dose should be rounded to the nearest vial size, and a second dose may only be ordered based on the serum uric acid level 12 hours after first dosing. Preliminary results showed one dose of rasburicase was effective in reducing serum uric acid in all patients and that there was no need for a second dose. Utilizing the guidelines resulted in a cost savings of $50,000 during the last three months.
CONCLUSIONS: Criteria-based guidelines for rasburicase use and dose rounding by pharmacists are effective means of ensuring optimal utilization of a high cost medication.

299. Evaluation of blood pressure and lipid control in pharmacist-managed diabetes patients. *Leigh Ann Ramsey, Pharm.D.,* Marshall Bouldin, M.D., Alison Ligon, B.S.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: To determine whether patients receiving diabetes medication management by pharmacists in an interdisciplinary Diabetes Management Clinic are attaining blood pressure and lipid parameter goals.
METHODS: Retrospective analysis of medical records of pharmacist-managed patients was performed. Three or more visits between August 1, 2000 and July 31, 2001 were required for selection. Records were reviewed for diagnoses of hypertension and dyslipidemia, initial and final blood pressure measurements, initial and final lipid parameters, and antihypertensive and lipid-lowering medication use.
RESULTS: 80 patients met eligibility criteria: 65.0% female, 62.5% African-American, initial BMI 34.0. Hypertension was documented in 75.0% of patients; 31.7% attained a systolic BP ≤ 130 and 60.7% a diastolic BP ≤ 80. Ninety-seven percent received antihypertensive medications: ACEI (74.1%), diuretic (53.4%), β-blocker (19.0%), non-dihydropyridine CCB (17.2%), dihydropyridine CCB (17.2%), ARB (12.1%), centrally-acting agent (6.9%), other (5.1%). Dyslipidemia was documented in 65%. Of these patients, 36.5% received medication: statin (84.9%), fibric acid derivative (15.8%), niacin (5.3%), bile acid sequestrant (5.3%). Documentation for no medication included in 73.8%: LDL at goal (46.7%), therapeutic lifestyle changes (46.7%), other (6.7%). Forty-three percent of patients with dyslipidemia achieved LDL <100.
CONCLUSIONS: Mississippi has the largest diabetes population in the United States; the majority fit criteria for metabolic syndrome. This innovative model, involving pharmacists in medication therapy management, is effective in glycemic control and compliance with standards of care; however, this study demonstrates the need for increased focus on blood pressure and lipid goals. Clinical outcomes observed will be used to expand medication therapy management in the DMC to include hypertension and dyslipidemia.

300. An academic detailing initiative to optimize the use of antimicrobials in acute rhino-bacterial sinusitis and pharyngitis in ambulatory care patients at a multispecialty ambulatory clinic. H. Eric Hughson, M.D., *Vincent J. Colucci, Pharm.D.,* Phillip R. Gardner, M.D., George F. Risi, M.D., C. Eugene Mead, Ph.D., Deb A. Overholtzer, R.N., Lynne M. Evans, R.N., Jean T. Carter, Ph.D., Pharm.D., Brant J. Goode, M.P.H., R.N.; University of Montana, Missoula, MT.

PURPOSE: Inappropriate antibiotic prescribing and antibiotic resistance in treating acute rhinobacterial sinusitis (ARBS), nasopharyngitis (NP), and uncomplicated viral upper respiratory tract illness (VURI) are important infectious disease issues. We established an internal quality improvement (QI) initiative at our 70-physician, multispecialty clinic regarding the use of antimicrobials and antimicrobial resistance. The goals of the project focused on: 1) optimizing antimicrobial use in ARBS and NP 2) diminishing indiscriminate antimicrobial use in uncomplicated VURI and 3) improving health-care provider and public education.
METHODS: Baseline primary care visit data for acute NP, ARBS, and acute URI were collected from May 2000 to May 2001. 380 charts were randomly selected and retrospectively reviewed for antimicrobial appropriateness using published criteria. Throughout the next year, educational and awareness efforts were made to providers and the public regarding antibiotic resistance using: 1) academic detailing 2) inservices, 3) media coverage, and 4) informational pamphlet handouts. After one year, a retrospective review of 320 randomly sampled charts from primary care visits (May 2001-May 2002) was again conducted for antibiotic prescribing habits and comparatively analyzed against baseline.
RESULTS: Chi-square analysis revealed the percentage of patients receiving antibiotics associated with the identified diagnoses decreased significantly from 71% (2001) to 55% (2002), p<0.001. The percentage of patients with non-sinusitis URI diagnoses remained relatively constant (76% [2001] vs 80% [2002], p=NS) but the percentage of those patients receiving antibiotics declined significantly from 62% to 46%, p<0.001. The use of treatments other than antibiotics (decongestants, cough suppressants, non-pharmacological agents, etc.) increased significantly from 60% to 76%, p<0.001.
CONCLUSIONS: This initiative suggests that a concerted academic detailing effort aimed at physicians, mid-levels, pharmacists and patients is likely effective at decreasing indiscriminate antibiotic use for ARBS, NP, and uncomplicated VURI.

301. Development of a cardiovascular wellness clinic by a clinical pharmacist practitioner in an interventional cardiologists' office. *Robert A. Ashworth, Pharm.D., CPP,* Stephen E. Kearney, Jr., Pharm.D., Steven C. Walden, Pharm.D., M.B.A.; Southeastern Heart and Vascular Center, Greensboro, NC; Pfizer, Inc., Raleigh, NC.; Pfizer, Inc., Lithia, FL.

PURPOSE: A clinical pharmacist practitioner was hired to develop cardiovascular wellness programs for a group of six interventional cardiologists. The program was to address anticoagulation, hypertension, hypercholesterolemia, and heart failure. This poster will describe the preparatory work to develop such a clinic and the impact on the practice to date.
METHODS: Charts were reviewed for patients meeting entry criteria (seen by cardiologist in last 2 years; labs obtained within 1 year) to determine a baseline evaluation. Data was placed in electronic databases (CHD Risk, Pfizer, Inc. and CoumaCare, BMS) for evaluation of INR/Blood Pressure/ LDL goal attainment, Framingham risk (including elements of heart failure), and ASA post-MI.
RESULTS: Of the 13,495 charts reviewed, 33% were lost to follow-up and 38% (n=5183) met criteria. Of these patients, approximately 13.8%, 98.8%, and 49.8% were able to be evaluated for INR, Blood Pressure, and LDL goal attainment, respectively. Framingham risk was calculated for 51%. There were 2703 males and 2480 females. The age range was 14-99 and the mean was 64. Of the 713 patients that were entered into CoumaCare, 439 were active patients and 65% were in range for INR. Blood Pressure goal was 30% of 5076 using 130/80, LDL was 65.75% of 2581 patients that had a documented LDL, and 578 patients did not have ASA post-MI.
CONCLUSIONS: Utilizing the CHD Risk and CoumaCare databases, this data will be used to educate the practice and to make system changes to improve adherence, patient care, and outcomes.

302. Clinical and economic outcomes associated with a chronic kidney disease clinic. *Melanie S. Joy, Pharm.D.,* Kimberly Dornbrook-Lavender, Pharm.D., BCPS, Amy Mottl, M.D., Ronald J. Falk, M.D.; University of North Carolina, Chapel Hill, NC.

PURPOSE: Chronic kidney disease (CKD) affects approximately 10 million persons in the U.S. Similar to end-stage renal disease, CKD patients have secondary complications from kidney dysfunction including anemia, iron deficiency, hyperphosphatemia, hyperparathyroidism, and uncontrolled hypertension, among others. We report the outcome measures of anemia management from the initial year of a pharmacist-directed CKD clinic.
METHODS: Patients with CKD requiring anemia management were evaluated, prescribed erythropoietic and iron therapy, and regularly monitored by a clinical pharmacist, in a collaborative practice of nephrologists. Patients were seen and evaluated at a frequency that was determined by their prescribed erythropoietic therapy. The clinical goals of anemia therapy were those defined by the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-DOQI): hemoglobin (Hgb) 11-12 g/dL, hematocrit (Hct) 33-36%, transferrin saturation (Tsat) ≥ 20%, Ferritin >100 µg/ml. Financial reports were generated quarterly to determine clinic profits based on patient visits and drug therapy administered.

	Baseline	Follow-up
Creatinine Clearance (ml/min)	29.4 ± 18	27.0 ± 15
Hgb (g/dL)	10.1 ± 1.5	11.1 ± 1.4
Hct (%)	30.2 ± 4.4	33.2 ± 3.8
Tsat (%)	23.8 ± 12.7	29.2 ± 12.4
Ferritin (µg/ml)	154.0 ± 122	168.3 ± 161

RESULTS: Within a year, the clinic grew from 30 to 83 patients, requiring 20% of the clinical pharmacist's effort. The demographic breakdown consisted of: gender (51% male; 49% female), race (52% Caucasian; 41% African-American; 3% Hispanic; 2% Asian, 1% not reported), age 65.7 ± 15 years, and weight 76.9 ± 20 kg. Diabetes and hypertension as the etiologies for CKD were present in 36% and 30% of patients, respectively. Patients were primarily prescribed darbepoetin alfa for anemia treatment and all received oral iron therapy at a target of 200 mg elemental iron per day. Darbepoetin alfa was prescribed (230 prescriptions) at the following dosing intervals and mean doses over the course of the previous year: Q2W (56.5 µg), Q3W (59 µg), Q4W (66 µg), and Q5W (55 µg). Results for the clinic baseline and follow-up key laboratory parameters are presented below (mean ± SD). Financial analysis of the profit margin for the erythropoietic agents administered and visit charges indicated a gross profit of $40,000 for the first year of the clinic. This resulted in a gross profit margin of $53,000 as compared to the previous year (prior to the initiation of a pharmacist-directed CKD clinic).
CONCLUSIONS: A pharmacist-directed CKD clinic can improve laboratory parameters to achieve the NKF-DOQI goals for the treatment of anemia. In addition, improved documentation of services and drug therapy management can provide a source for additional clinical revenue.

303. Pediatric Medication Safety Task Force: A multidisciplinary working group created to make recommendations that will enhance the safety of medication use in pediatric inpatients. *Christine A. Robinson, Pharm.D.,* Kevin Slavin, M.D., Robert Fakelmann, R.Ph. M.B.A.; Hackensack University Medical Center, Hackensack, NJ.

PURPOSE: The pediatric medication process is a unique and challenging system. In response to a documented increase in pediatric medication errors at Hackensack University Medical Center (HUMC), the Pediatric Medication Safety Task Force (PMSTF) was assembled. The mission of this multidisciplinary working group was to evaluate all stages of the medication management system of inpatient pediatric units at HUMC and to utilize Failure Mode and Effect Analysis (FMEA) to make recommendations that will reduce the Risk Product Number (RPN).

METHODS: PMSTF met twice monthly from April 11, 2002 to April 8, 2003. The task force meetings were structured initially to educate members of national data regarding safe medication practices and FMEA methodology. An FMEA was then developed that represents the actual and potential failures that occur in the HUMC pediatric medication system. This was organized in a sequential format that evaluated all steps of the medication system, from the decision to prescribe through therapeutic drug monitoring. PMSTF was then divided into three multidisciplinary subcommittees, which reviewed the FMEA and recognized best-demonstrated practices.
RESULTS: The final combined recommendations from the subcommittees were completed and organized by category—necessary infrastructure, environment of care, culture of safety, medication processes and education of clinical staff. The final report was presented to the HUMC Pediatric Service Line to facilitate development of implementation plans.
CONCLUSIONS: FMEA is a proactive tool for identifying sources of potential error. Based on the PMSTF recommendations, multidisciplinary committees are being created to address recognized areas of concern and enhance medication safety.

304E. Implementation of a coordinating council as an academic pharmacy practice department management model. Laurie L. Briceland, Pharm.D., Robert A. Hamilton, Pharm.D., Aimee F. Strang, Pharm.D., Darren M. Triller, Pharm.D., *Nancy M. Waite, Pharm.D.,* Mary H. Andritz, Pharm.D.; Albany College of Pharmacy, Albany, NY.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, Minneapolis, MN, July 22, 2003.

305. Evaluation of a newly established pharmacotherapy clinic's impact on diabetes management. *Dana G. Carroll, Pharm.D., BCPS*; University of Oklahoma, Tulsa, OK.

PURPOSE: A pharmacist managed pharmacotherapy referral clinic was established in the fall of 2001 at the OU–Tulsa Family Medicine Clinic. The goal of this project was to assess the impact of the referral clinic on diabetes management according to ADA standards.
METHODS: The study period was from November 2000 to October 2002. Patients served as their own control. Data was collected by a retrospective chart review. Inclusion criteria included: OU–Tulsa Family Medicine referred patients, greater than or equal to 18 years of age, diagnosis of DM type 2, and a minimum of one visit to the pharmacotherapy clinic during the period of November 1, 2001 to October 31, 2002.
RESULTS: Sixty-three patients met inclusion criteria. In the year prior to entering the pharmacotherapy clinic, 31% of patients had at least one $HgbA_{1c}$ assessed. After referral to the pharmacotherapy clinic, 95% of patients had at least one $HgbA_{1c}$ assessment and 54% of patients had multiple $HgbA_{1c}$ values. Seventy-four percent of referred patients achieved a mean reduction of 2.24% in $HgbA_{1c}$. Twenty percent experienced an increase in $HgbA_{1c}$ while 6% experienced no change. Twenty-two percent of patients, averaging 5 clinic visits, achieved and maintained goal $HgbA_{1c}$ values at the end of the study period. Patients not achieving goal $HgbA_{1c}$ had an average of 2.29 visits.
CONCLUSIONS: A pharmacist managed pharmacotherapy clinic increased the frequency of $HgbA_{1c}$ assessment and achieved considerable reductions in $HgbA_{1c}$ values. Achievement of goal $HgbA_{1c}$ was influenced by the frequency of patient visits.

306. Sever acute respiratory syndrome (SARS) outbreak: the pharmacist role in an academic tertiary care hospital. *Tom Chin, B.Sc.Phm., Pharm.D.,* Rosemary Tanzini, B.Sc.Phm., Janice Wells, B.S.P., Pharm.D.; St. Michael's Hospital, Toronto, ON, Canada.

PURPOSE: To describe the acquired responsibilities of pharmacists during the SARS outbreak.
METHODS: Literature search was conducted about appropriate use of drugs recommended by infectious diseases specialists of the affected hospitals. Relevant procedures and protocols were developed: drug dosing and administration, drug procurement, and modification to the drug delivery system.
RESULTS: A SARS information kit was developed and it contained the management algorithm, drug dosing and procurement procedures. Dosing and administration guidelines for intravenous ribavirin were developed as it was not marketed in Canada and was used for an un-approved indication. Its use was subsequently discontinued because of insignificant response and high toxicity rate. Participation in a trial on interferon-alphacon1 was initiated. Guidelines on switching from nebulized to inhaled medications were developed. Current drug distribution procedures were modified and new ones developed to meet more stringent infection control standards. The various protocols and procedures underwent constant updates as new information was learned. Education and constant update of pharmacists was crucial. There was regular e-mail communication among pharmacists in various hospitals.
CONCLUSIONS: Pharmacists played a vital role during the management of the SARS crisis in the areas of drug information, access to non-marketed drugs, drug dosing protocol development and special handling of drug delivery. Lessons learned could be adapted for future crises needing pharmacy support.

307. Recombinant factor VIIa attenuates bleeding due to enoxaparin. *Judith L. Kristeller, Pharm.D.*; Wilkes University, Wilkes-Barre, PA.

PURPOSE: To report a case of enoxaparin-induced bleeding treated with recombinant factor VIIa (rVIIa).
CASE SUMMARY: A 74-year-old 83 kg white male with acute renal failure was treated for a NQWMI with enoxaparin 80 mg SQ Q12 hours for six days and subsequently developed a massive rectus sheath hematoma requiring surgical exploration. Post-operatively he developed hemorrhagic shock and the hematocrit decreased from 14 g/dL down to 6.1 g/dL despite 8 units PRBC, 8 units FFP, one pooled platelet concentrate, vitamin K 10 mg IV and protamine 40mg IV. Within 3 hours of receiving rVIIa 50 ug/kg and 4 units of PRBC, his hematocrit increased to 12 g/dL and bleeding from his abdominal wound stopped. Approximately 8 hours after the first dose of rVIIa, his abdominal dressings were once again blood-soaked and his hematocrit dropped, requiring a second dose of rVIIa. The patient received 2 subsequent doses of rVIIa approximately every 3 hours for a total of 4 doses after which he stabilized.
CONCLUSIONS: Recombinant factor VIIa increases thrombin generation at the site of vascular injury. However, its short half-life of 2.3 hours can predispose patients to rebleeding. In the extrinsic pathway, rVIIa complexes with factor X to form Xa, which could theoretically overcome the inhibition of Xa by enoxaparin. Considering the cost of rVIIa (NovoSeven®) is approximately $7,100 per 4.8 mg vial, rVIIa drug cost for this patient exceeded $28,000. In conclusion, rVIIa can potentially reverse bleeding due to enoxaparin, however with significant financial implications.

308. Comprehensive diabetes management: a clinical pharmacy practitioner as a means to improve the health care report card. *Cassandra D. Benge, Pharm.D.,* R. Shane Greene, Pharm.D.; South Texas Veterans Health Care System, San Antonio, TX; University of Texas at Austin, Austin, TX; University of Texas Health Science Center, San Antonio, TX; Texas Tech Health Sciences Center, Dallas, TX.

PURPOSE: In recent decades, diabetes care has undergone fundamental modifications that have affected the manner in which patients are managed; these include (a) acceptance of strict metabolic control; (b) emphasis on primary care management; and (c) importance of cost containment. Due to the significant number of patients diagnosed with diabetes, it is difficult for a solo practitioner, despite the support of a diabetes patient education team, to adhere to the ADA Standards of Medical Care.
METHODS and RESULTS: In 1998 at the satellite clinic division of the South Texas Veterans Health Care System, the traditional diabetes team, which primarily focused on education, was restructured to include a clinical pharmacy specialist with prescribing privileges and a clinical scope of practice. The goal was to more rapidly facilitate glycemic control for all referred patients. By 1999, clinical pharmacy services expanded to include management of the components of the metabolic syndrome in diabetic patients. 822 patients have been evaluated; 492 patients have seen ≥ 2 times secondary to poor glycemic control.
CONCLUSIONS: It is anticipated that clinical pharmacy services will increase measurement of process indicators, facilitate reduction in hemoglobin A1c, blood pressure, and lipoprotein profile, and increase utilization of renoprotective and cardioprotective prescriptions. Currently, a retrospective chart review is ongoing and will evaluate the quality of care to a non-random sample of 200 male and female diabetic patients with a baseline hemoglobin A1c ≥ 8.0 and who required follow-up for an approximate one year period. between October 10, 1999 and June 30, 2003.

309. Which one comes first? Development of a chemotherapy administration sequence chart. *Brad L. Stanford, Pharm.D., BCOP,* Stacey D. Zondor, Pharm.D., Shalyn Kennedy, Pharm.D.; Texas Tech University Health Sciences Center, Lubbock, TX.

PURPOSE: Combination chemotherapy is the mainstay of treatment for a variety of malignancies. The sequence of chemotherapy administration can be important due to effects on efficacy, toxicity, and pharmacokinetics. Although many reports have been published on this subject, there is, to our knowledge, no single source that describes the best sequence of administration for various chemotherapy regimens. Therefore, we developed a sequencing chart as a tool for health care personnel at our institution.
METHODS: A literature search was conducted to identify human studies that specifically compared various chemotherapy regimen sequences. Studies were assessed for differences in sequence-dependent toxicity, efficacy, and pharmacokinetics. All authors reviewed all studies to arrive at a consensus for development of the sequencing chart.
RESULTS: A total of 37 studies evaluating 22 different regimens were identified for inclusion in the chart. Sequence dependent interactions were categorized as follows: 11 toxicity, 6 pharmacokinetic, 2 efficacy. Five of these interactions were assigned to multiple categories, the most common of which was toxicity and pharmacokinetic. Of the identified studies, no differences due to sequence were found in 8 regimens.
CONCLUSIONS: Improper sequence of administration of certain

chemotherapeutic agents may result in increased toxicity, decreased efficacy, as well as pharmacokinetic differences of unclear significance. For this reason, our sequencing chart serves as a valuable resource for health care personnel and assists in improved patient outcomes.

310. Critical care pharmacy services: a nation-wide survey. *Sirada Maphanta, Pharm.D.*, Jeffrey T. Fish, Pharm.D., BCPS; University of Wisconsin, Madison, WI.

PURPOSE: To characterize pharmacy services in intensive care units (ICUs) according to scope of practice outlined by the task force on critical care pharmacy services (CCPS) in 2000.
METHODS: A 43 question-survey was developed using activities outlined in the position paper on CCPS. The questions were divided into patient care, documentation, research, education, and administration domains. The survey was electronically mailed to pharmacists practicing in ICUs within the U.S. and Canada identified through the ACCP critical care practice and research network.
RESULTS: The survey achieved a response rate of 24% (43/181). Forty-nine percent were from community hospitals and 42% were from academic medical centers (AMCs). The size of the institutions ranged from 82 to 1450 licensed beds with the mean hospital and ICU census of 374 and 40 patients, respectively. Of 43 total activities, a mean of 31 (72%, range 12-43) was accomplished. Fourteen institutions (33%) achieved the entire 18 fundamental activities, while 3 (7%) and 1 (2.3%) institutions attained the entire 13 and 12 desired and optimal activities, respectively. The average numbers of fundamental, desired, and optimal activities performed by these institutions were 16 (range 7-18), 9 (range 4-13), and 6 (range 0-12), respectively. AMCs or larger institutions achieved higher number of desired and optimal activities ($p<0.05$), as well as performed more activities in research and education domains.
CONCLUSIONS: Critical care pharmacist activities could be improved by ensuring all fundamental activities outlined in the scope of practice are performed and expanding to higher level of teaching and research activities.

STUDENT, RESIDENT, FELLOW RESEARCH IN PROGRESS

These papers describe original research by students, residents, and fellows in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, pharmacoepidemiology and pharmacogenomics in which the research effort is still on-going. The abstract title and authors are published in *Pharmacotherapy*; the full abstract will be published in the meeting program book.

311. Efficacy and economic evaluation of a volume-based Cathflo Activase® protocol versus a fixed-dose alteplase protocol for catheter occlusions in pediatric patients. *Jennifer A. Norberg, Pharm.D.,* Allison M. Chung, Pharm.D., Rosa Vidal, M.D., Cheryl Falkos, M.D.; University of Florida, Gainesville, FL; University of South Alabama Children's and Women's Hospital, Mobile, AL.

312. A comparative evaluation of oral valganciclovir for CMV prophylaxis in transplant patients. *Renee R. Weng, Pharm.D.,* LanChi L. Bui, Pharm.D., Winnie Huang, M.D., Sean Cao, M.D.; University of California Medical Center, Orange, CA.

313. Student perceptions of didactic curricular time spent on pain management, peptic ulcer disease, and diabetes. *Michelle C. Lenart, Pharm.D.,* Jared M. Downing, Pharm.D., Dong-Churl Suh, Pharm.D., Robert Colucci, Pharm.D., John Messina, Pharm.D.; Rutgers University, Piscataway, NJ; Purdue Pharma L.P., Stamford, CT.

314. Impact of pharmacist education on asthma management. *Divya T. Desai, Pharm.D.,* Catherine Woodard, Pharm.D., Douglas Roblin, Beth Barham, Pharm.D., Rina Patel, Pharm.D.; Kaiser Permanente, Atlanta, GA; Merck and Co., Inc., Whitehouse Station, NJ.

315. Vitamin D and skeletal health in older veterans receiving phenytoin or carbamazepine monotherapy. Mary E. Elliott, Pharm.D., Ph.D., Barry E. Gidal, Pharm.D., John C. Jones, M.D., Philip J. Kurle, M.D., *Shannon K. Parker, Pharm.D.,* Jessica L. Praska, Pharm.D.; University of Wisconsin; Veterans Affairs Medical Center, Madison, WI.

316. Steady-state pharmacokinetics and pharmacodynamics of cefepime administered every six hours in critically ill patients. *Sarah D. Hittle, Pharm.D.,* David W. Smith, Pharm.D., S. Christian Cheatham, Pharm.D., Tate N. Trujillo, Pharm.D., Matthew F. Wack, M.D., Michael B. Kays, Pharm.D., BCPS, FCCP; Clarian Health Partners, Inc.; Methodist Hospital; Infectious Diseases of Indiana; Purdue University, Indianapolis, IN.

317. Characterization of multiple-dose dolasetron for treatment of post-operative nausea and vomiting in a university hospital setting. *Kimberly J. Novak, Pharm.D.,* Ann B. Amerson, Pharm.D., Heather H. Cornett, Pharm.D., Gary D. Coutts, R.Ph., Kenneth E. Record, Pharm.D., Kelly M. Smith, Pharm.D.; University of Kentucky Chandler Medical Center, Lexington, KY.

319. Hemodialysis drug clearance: evaluation of four cephalosporins. *Jennifer Rais, Pharm.D.,* Jennifer Maple, Pharm.D., Terry Dunn, Pharm.D., Mark Wolf, M.D., Irfan Omar, M.D.; Detroit Medical Center; Sinai-Grace Hospital, Detroit, MI.

320E. Nosocomial pneumonia and related complications in the critically ill trauma patient: Does choice of proton pump inhibitor versus histamine antagonist influence infection? *Stephanie Mallow, Pharm.D.,* Jill A. Rebuck, Pharm.D., BCPS, Turner Osler, M.D., FACS, John Ahern, Pharm.D., BCPS, Mark A. Healey, M.D., FACS, Fredrick Rogers, M.D., FACS; Fletcher Allen Health Care, Burlington, VT.

Published in Critical Care Medicine 2002;30(12):A118.

321. Assessment of leukocyte function using ^{18}F-fluorodeoxyglucose. *LeHuyen Trinh, Pharm.D.,* Lynn M. Kaczmarek, B.S., Joseph W. Vilani, M.S., Hani A. Nabi, M.D., Ph.D., Edward M. Bednarczyk, Pharm.D.; University at Buffalo, Buffalo, NY.

322. Development, implementation, and data collection of a community pharmacy-based hypertension monitoring clinic. *Peter M. Brody Jr., Pharm.D.*; State University of New York at Buffalo, Buffalo, NY.

323. Evaluation of the impact of the media on continuation of hormone replacement therapy in postmenopausal women in a community setting. *Chris Bode, R.Ph., Pharm.D. candidate,* Patricia A. Rozek, Pharm.D., BCPS; University of Cincinnati, Cincinnati, OH.

324. Evaluation of β-blocker therapy in systolic heart failure patients in an outpatient family medicine clinic. *Amy Hein, R.Ph., Pharm.D. candidate,* Patricia Rozek, Pharm.D.; University of Cincinnati, Cincinnati, OH.

325. Assessment of osteoporosis screening in Medicare patients in an outpatient family medicine clinic. *Rashmika Moradia, R.Ph., Pharm.D. candidate,* Patricia A. Rozek, Pharm.D., BCPS; University of Cincinnati, Cincinnati, OH.

326. Assessment of the change from imipenem/cilastatin to cefepime in adult patients with febrile neutropenia. *Alison M. Massaro, Pharm.D.,* Philip Hall, Pharm.D., BCPS, BCOP; Medical University of South Carolina, Charleston, SC.

327E. Evaluation of the incidence of diabetes mellitus associated with the use of atypical antipsychotics in non-schizophrenic patients in a VA outpatient clinic. *Ellen C. Strapp, Pharm.D.,* Chris R. Frei, Pharm.D., Cassandra D. Benge, Pharm.D.; South Texas Veterans Health Care System; University of Texas Health Science Center, San Antonio, TX.

resented at the Alcalde Southwest Leadership Conference, Arlington, TX, April 2003.

328. Use of gabapentin for neuropathic pain in the long-term care setting. *Nicole L. McMaster, Pharm.D.,* Sharon A. Jung, Pharm.D., BCPS; South Texas Veterans Health Care System, San Antonio, TX.

329. Comparison of two ceftriaxone dosage regimens in adult patients with community-acquired pneumonia. *Jarrett R. Amsden, Pharm.D.,* Douglas Slain, Pharm.D., BCPS; West Virginia University Hospitals, Morgantown, WV.

RESEARCH INSTITUTE

The following papers, based on Fellowships and Research Awards provided by the ACCP Research Institute, will be presented. Full titles and authors are listed, although a complete abstract may not be available for all papers at the time of this printing.

330. ACCP Pharmacotherapy Research Award: Effects of VSL#3 on P-glycoprotein mediated oral drug absorption. *Brien L. Neudeck, Pharm.D.*, Jennifer M. Loeb; University of Wisconsin, Madison, WI.

331. Amgen Biotechnology Research Award: Clinical and economic outcomes of epoetin alfa therapy in critically ill patients. *Sandra L. Kane-Gill, Pharm.D., M.S.*, Emily E. Castelli, Pharm.D., Levent Kirisci, Ph.D., Ted L. Rice, Pharm.D., Mitch P. Fink, M.D.; University of Pittsburgh, Pittsburgh, PA.

332. AstraZeneca Cardiovascular Research Award: Pharmacokinetic interaction between warfarin and ginseng. *Thomas L. Lenz, Pharm.D.,* Christopher J. Destache, Pharm.D., FCCP, Michele A. Faulkner, Pharm.D., Kathleen A. Packard, Pharm.D., Daniel E. Hilleman, Pharm.D., FCCP, Amy J. Arouni, M.D., Michael S. Monaghan, Pharm.D.; Creighton University Medical Center, Omaha, NE.

333. Aventis Allergy/Asthma Research Award: Effect of inhaled steroid therapy on tracheal aspirate cytokine concentrations in very low birth weight infants at risk for chronic lung disease. *Kim G. Adcock, Pharm.D.,* Jeremy R. Martin, B.S., R.J. Baier, M.D.; University of Mississippi, Jackson, MS; Louisiana Health Sciences Center, Shreveport, LA.

334. Aventis Allergy/Asthma Research Award: Pharmacists behavioral control and pediatric asthma counseling. *Francoise G. Pradel, Ph.D.,* Mona Tsoukleris, Pharm.D., Nour Obeidat; University of Maryland, Baltimore, MD.

335. Aventis Infectious Diseases Research Award: Functional genomics of high-level azole antifungal resistance. *P. David Rogers, Pharm.D., Ph.D.,* Katherine S. Barker, Ph.D.; University of Tennessee, Memphis, TN.

336. Aventis Infectious Diseases Research Award: Vancomycin crystalline degradation product can help select and maintain *Staphylococcus aureus* strains with reduced susceptibility to vancomycin. *Jeffrey R. Aeschlimann, Pharm.D.*; University of Connecticut, Storrs, CT; University of Connecticut Health Center, Farmington, CT.

337. Bristol-Myers Squibb Primary Care Research Award: LDL cholesterol and C-reactive protein changes with low-dose of fluvastatin, lovastatin, and pravastatin in hyperlipidemia. *Joseph J. Saseen, Pharm.D., BCPS,* Sheryl L. Follin, Pharm.D., BCPS, W. Troy Donahoo, M.D., Kavita Nair, Ph.D.; University of Colorado Health Sciences Center, Denver, CO.

338. Roche Transplantation Research Award: Calcineurin activity as a marker of immunosuppression. *Yi-Min (Julie) Ku, M.S., Pharm.D.,* Julie A. Stoner, Ph.D., Paul Stemmer, Ph.D., Nabil G. Guirguis, M.D.; University of Nebraska Medical Center, Omaha, NE; Wayne State University, Detroit, MI; Institute of Environmental Health Sciences, Detroit, MI.

339. Roche Transplantation Research Award: P-glycoprotein localization and expression in drug-induced nephrotoxicity. *Melanie S. Joy, Pharm.D.,* Volker Nickeleit, M.D., Susan L. Hogan, Ph.D., William F. Finn, M.D.; University of North Carolina, Chapel Hill, NC.

340. TAP Pharmaceutical Products Gastrointestinal Research Award: Effects of U50488 on colonic inflammation in mice. *Brien L. Neudeck, Pharm.D.,* Jennifer M. Loeb; University of Wisconsin, Madison, WI.

341. Wyeth Women's Health Care Research Award: Tissue factor polymorphisms in postmenopausal women. *Kai I. Cheang, Pharm.D., BCPS,* Heather M. Sturgill, B.S., Patricia W. Slattum, Pharm.D., Ph.D., John N. Clore, M.D.; Virginia Commonwealth University; Richmond, VA.

342. Aventis Infectious Diseases Fellowship: Sex-based differences in the disposition of levofloxacin. *Brian R. Overholser, Pharm.D.,* Michael B. Kays, Pharm.D., Seema Lagvankar, D.O., Mitchell Goldman, M.D., Kevin M. Sowinski, Pharm.D.; Purdue University; Indiana University, Indianapolis, IN.

343. Aventis Oncology Fellowship: Phase I study of epothilone B analog BMS 247550 in combination with carboplatin in recurrent and/or refractory solid tumors. *Ollie Anum, Pharm.D.,* Anne Dellaportas, B.S., Barbara Padilla, B.S., Daniel M. Sullivan, M.D., Kapil Bhalla, M.D., Richard Lush, Ph.D.; H. Lee Moffitt Cancer Center, Tampa, FL.

344. Bayer Critical Care Fellowship: Alterations in drug absorption during critical illness: the role of the peptide transporter, PEPT1. *Jeffrey P. Gonzales, Pharm.D.,* David R. Foster, Pharm.D., Lynda S. Welage, Pharm.D., FCCP; Cleveland Clinic Foundation, Cleveland, OH; Purdue University, Indianapolis, IN; University of Michigan, Ann Arbor, MI.

345. Bayer Critical Care Fellowship: Cardioprotective effects of losartan during myocardial ischemia-reperfusion injury. *Jeremy D. Flynn, Pharm.D.,* Ginell R. Post, M.D., Ph.D., Wendell S. Akers, Pharm.D., Ph.D.; University of Kentucky, Lexington, KY.

347. Bayer Critical Care Fellowship: Longitudinal solute clearance in an in vitro continuous venovenous hemofiltration model. *Deborah A. Pasko, Pharm.D.,* Bruce A. Mueller, Pharm.D., FCCP, BCPS; University of Michigan, Ann Arbor, MI.

348. Merck Cardiovascular Fellowship: Effects of atorvastatin on low-density lipoprotein phenotype and C-reactive protein in chronic dialysis patients. *Kimberly A. Dornbrook-Lavender, Pharm.D. BCPS,* John A. Pieper, Pharm.D., BCPS, FCCP, Melanie S. Joy, Pharm.D.; University of North Carolina, Durham, NC; University of New Mexico, Albuquerque, NM.

349. Merck Cardiovascular Fellowship: What is the impact of elevated catecholamine concentrations on the defibrillation threshold in patients with implanted cardioverter-defibrillators. *James S. Kalus, Pharm.D., BCPS,* Michael F. Caron, Pharm.D., Jeffrey Kluger, M.D., Danette Guertin, M.S.N., Brian F. McBride, Pharm.D., C. Michael White, Pharm.D.; University of Connecticut, Storrs, CT; Hartford, Hospital, Hartford, CT; University of Rhode Island, Birmingham, RI.

350. Merck Pharmacoeconomics and Outcomes Fellowship: Validation of four clinical indicators of preventable drug-related morbidity. *Priti S. Flanagan, Pharm.D.,* Neil J. MacKinnon, Ph.D., Susan K. Bowles, Pharm.D., Susan A. Kirkland, Ph.D.; Dalhousie University, Halifax, NS, Canada.

351. Ortho Biotechnology Oncology Fellowship: Genetic polymorphisms of CYP2C19 associated with patients treated with thalidomide in a phase III trial for androgen-dependent prostate cancer. *Michael C. Cox, Pharm.D.,* Matthew Permenter, B.S., Douglas K. Price, Ph.D., William Dahut, M.D., William D. Figg, Pharm.D.; National Cancer Institute, Bethesda, MD.

352. Ortho-McNeil Infectious Diseases Fellowship: Pharmacokinetics, safety, and efficacy of a triple-protease inhibitor salvage regimen containing amprenavir, saquinavir, and ritonavir. *Amanda H. Corbett,* Joseph J. Eron, Susan A. Fiscus, Naser L. Rezk, Melissa M. Diebold, Angela D.M. Kashuba; University of North Carolina, Chapel Hill, NC.

353. Roche Transplantation Fellowship: P-glycoprotein expression and activity on T-lymphocytes of solid organ transplant recipients. Eva M. Vasquez, Pharm.D., *Vanessa A. Mategrano, Pharm.D.,* Yevgeniya Petrenko, M.D., Ph.D., Nicole M. Sifontis, Pharm.D., Enrico Benedetti, M.D.; University of Illinois, Chicago, IL.

354. Wyeth Psychopharmacy Fellowship: Assessment of serotonin type 1A ($5\text{-}HT_{1A}$) receptor genotype in a normal versus a depressed population and the relationship to predictability of antidepressant responsiveness. *Toya M. Bowles, Pharm.D., BCPP,* Gary M. Levin, Pharm.D., BCPP, FCCP, Taimour Y. Langaee, Ph.D., Jennifer Y. Tan, Pharm.D., BCPP, Hossein N. Yarandi, Ph.D., Julie A. Johnson, Pharm.D., BCPS, FCCP, William J. Millard, Ph.D.; Organon Pharmaceuticals USA Inc, Savannah, GA; University of Florida, Gainesville, FL; North Star Behavioral Hospital, Anchorage, AK.

355. Wyeth Psychopharmacy Fellowship: The association of serum anticholinergic activity with delirium and measures of attention and confusion in elderly nursing home residents. *Ryan M. Carnahan, Pharm.D.,* Paul J. Perry, Ph.D., Brian C. Lund, Pharm.D., M.S., Kennith Culp, Ph.D.; University of Iowa, Iowa City, IA; Leureate Psychiatric Clinic and Hospital, Tulsa, OK.

2003 ACCP Annual Meeting Abstracts

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