ABSTRACTS

American College of Clinical Pharmacy
2002 Annual Meeting
October 20–23 ▪ 2002
Hyatt Regency Albuquerque
Albuquerque Convention Center
Albuquerque ▪ New Mexico

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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 2002 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. Development of a new taxonomy to classify clinical pharmacy recommendations. *Angela B. Hoth, Pharm.D.,* Barry L. Carter, Pharm.D., FCCP, BCPS, Cynthia K. Schulte, Pharm.D. candidate, Jose Ness, M.D., Ronald I. Shorr, M.D., Gary E. Rosenthal, M.D., Peter J. Kaboli, M.D.; Veterans Administration Medical Center; University of Iowa, Iowa City, IA.

PURPOSE: Development and reliability testing of a taxonomy to classify clinical pharmacy recommendations.
METHODS: The taxonomy categorized recommendations according to the problem type that prompted an intervention and the response required to implement a recommendation. Six problem categories (pharmaceutical issues, risk to patient, medication/indication issues, efficacy issues, cost, record update) were subdivided into 18 unique categories to identify a specific therapeutic problem addressed in a recommendation. Twelve response categories required to enact the recommendation were used. Each recommendation required a single problem and response category. Seven reviewers (3 Pharm.D.s, 4 M.D.s) categorized recommendations from a random sample of patients evaluated by a clinical pharmacist between 7/1/01 and 5/31/02. Inter-rater reliability was determined for each reviewer pair and the group using the κ statistic. Time to categorize recommendations was also recorded.
RESULTS: Reviewers categorized 146 recommendations for 21 patients (mean 7; range 1-17). Inter-rater agreement for the 18 therapeutic problem subcategories was good (overall κ=0.50, range 0.29-0.66). Greatest agreement occurred between Pharm.D. reviewers (κ=0.60) followed by Pharm.D.-M.D. pairs (κ=0.51) and M.D. pairs (κ=0.42). Reliability improved at the level of the six therapeutic categories (overall κ=0.54, median 0.62, range 0.29-0.71). Inter-rater agreement for the 12 response categories was high (overall κ=0.72, range 0.67-0.81). Completion of categorization averaged 4.6 minutes per patient (range 1-11.2).
CONCLUSION: This taxonomy provides a reliable method to evaluate clinical pharmacy recommendations based on the therapeutic problem and specific action recommended. This tool may be used clinically and in research to document clinical pharmacy activities in a standardized format.

2. Influence of the Internet on ACCP membership. *Susan Miller, Pharm.D.,* Julie Wright, Pharm.D., BCPS; University of Missouri at Kansas City, Kansas City, MO.

PURPOSE: The 2003 ACCP membership goal is to increase its members by 44%. ACCP must reach a diverse pharmacist population who may be naïve to its organizational mission and goals. Due to extensive Internet use by pharmacists, ACCP's Web page accessibility was evaluated.
METHODS: Using 8 distinct terms included in ACCP's mission statement, we searched the top 10 Internet search engines, rated by audience reach, to measure the frequency of encountering the ACCP site within the first 50 results. From the first 20 results of each search, the number of Web sites that link to pharmacy organizations, and subsequently link to ACCP, was determined. Additionally, ACCP link accessibility was determined among other pharmacy related Web sites including: academic institutions, credentialing and licensing boards, national organizations, and popular pharmacy journals.
RESULTS: The incidence of ACCP Web page appearance in the first 50 results was greatest with the search terms "clinical pharmacy" (100%) and "pharmacy advocacy" (90%). Twenty four percent of searches resulted in links to professional pharmacy organizations. Sixteen percent included an ACCP link. The proportion of Web sites with links to ACCP were: national organizations 100%, journals 50%, student organizations 38%, pharmacy schools 24% and credentialing/licensing boards 7%. Links consistently worked, but few (8%) included a description of ACCP.
CONCLUSIONS: Enhanced Internet exposure could increase ACCP membership. Enhanced exposure should be pursued through requests to post ACCP links on all pharmacy school and state boards of pharmacy Web sites, promotion of Web site link reciprocity among professional organizations, and ACCP Web site optimization to maximize priority listings from search engines.

Adverse Drug Reactions/Drug Interactions

3. Comparison of the specificity and sensitivity of five commonly available personal data assistant-based drug-drug interaction screening programs. *John R. Horn, Pharm.D., FCCP,* Philip D. Hansten, Pharm.D., Amy Kiesel, Pharm.D., Chi Nguyen, Pharm.D., Susan Lakey, Pharm.D.; University of Washington, Seattle, WA.

PURPOSE: To evaluate the specificity and sensitivity of drug-drug interaction screening programs commonly available on hand-held personal data assistants (PDAs).
METHODS: Twenty-one drug pairs were selected from patient medication profiles. Selected drugs pairs represented potentially significant (could harm patient) interactions, non-interacting drug pairs, and pairs exhibiting desirable pharmacodynamic interactions. Five PDA-based programs (Ifacts, MosbyIx, DrDrugs, PEPID PDC, Epocrates) were obtained from their providers. Each program was examined for the presence or absence of an interaction for each drug pair. Both drugs in each pair were individually searched to determine search engine proficiency. Interaction results were compared to a standard drug interaction reference (Hansten and Horn). The sensitivity (proportion of true positives) and specificity (proportion of true negatives) was calculated for each program.
RESULTS: Of the 21 pairs of drugs, 15 represented potentially significant interactions and six were either non-interacting pairs or of minimal clinical importance. The mean (range) sensitivity of the PDA programs was 0.63 (0.4-0.87); the mean (range) specificity was 0.6 (0.17-0.83). For comparison, the Physicians Desk Reference (PDR 2002 edition) had a sensitivity and specificity for these same interactions of 0.33 and 0.50, respectively. Of the 21 interactions, the PDA programs agreed with the reference standard on an average of 13 (62%) of the interactions (range 9-15).
CONCLUSIONS: Using PDA-based drug interaction references for patient management should be approached with caution. While these programs are generally superior to the PDR as a source of drug interaction information, users should be aware of the limitations of these programs as surrogates for standard drug interaction references and good clinical judgment.

4. Safety of concomitant treatment with moxifloxacin and selective serotonin reuptake inhibitors. *Shurjeel H. Choudhri, M.D.,* Daniel Haverstock, M.S., Frank Kruesmann, Ph.D.; Bayer Corporation, West Haven, CT; Bayer AG, Wuppertal, Germany.

PURPOSE: To compare the safety profile of IV and PO moxifloxacin (MXF) with that of comparator antibiotics (COMP) in patients receiving concomitant therapy with selective serotonin reuptake inhibitors (SSRIs).
METHODS: Data were pooled from 27 global, randomized, controlled MXF trials. WHO-DD codes were used to identify all patients who had received concomitant therapy with an SSRI and MXF or COMP. Comparators used most frequently in PO studies were cefuroxime, clarithromycin, cephalexin and amoxicillin while alatrofloxacin/trovafloxacin, levofloxacin and the combination of amoxicillin/clavulanate and clarithromycin were the comparators in the IV studies. Study population was subdivided into 4 groups: MXF, MXF + SSRI, COMP, COMP + SSRI. CPMP criteria were used to identify QTc outliers.
RESULTS: Of the 12,788 patients included in the analysis, 450 took at an SSRI concomitantly with antibiotic therapy (238 on MXF, 212 on COMP). Paired ECGs were available for 100 (55 MXF, 45 COMP) of these patients. The mean QTc change was +4 and +5 msec in the PO and IV MXF +SSRI groups respectively compared to a mean change of +6 and +3 in the PO and IV MXF groups. No QTc outliers were identified in either the PO or IV MXF ± SSRI patients. The incidence of cardiovascular adverse events was similar between the 4 groups.
CONCLUSIONS: The mean QTc interval change was similar for patients who were treated with IV or PO MXF alone or MXF + SSRI. The cardiovascular safety profile of moxifloxacin was not significantly affected by concomitant therapy with SSRIs.

6. Reliability and validity of Naranjo criteria for adverse drug event detection in the intensive care unit. *Sandra L. Kane, Pharm.D., M.S.*, Joseph F. Dasta, M.S., FCCM, Philip J. Schneider, M.S., Emmett McGuire, M.D., Lori Myers, M.D., Dev S. Pathak, D.B.A.; University of Pittsburgh, Pittsburgh, PA.

PURPOSE: The Naranjo scale has not been evaluated in critically ill patients. Hence, reliability and validity of the Naranjo criteria for assessing ADEs in critically ill patients was studied.
METHODS: Abnormal laboratory values were reviewed to identify ADEs during a 3-month period in a 38-bed surgical ICU. ADEs were classified into possible, probable and definite categories by a pharmacist. In cases of uncertainty, a panel of three experts was convened. Four raters independently reviewed the same ADEs using the Naranjo criteria to test inter-rater (between raters) reliability; reported as a κ statistic. Raters used the Naranjo criteria again 3-4 weeks later and a weighted κ statistic was calculated for test-retest reliability. Naranjo criteria were compared to expert opinion for criterion validity for each rater; reported as a κ statistic and Spearman rank (r_s) coefficient.
RESULTS: κ statistic between raters ranged from 0.144-0.479. Weighted κ ranged from 0.5402-0.9371 for test-retest reliability. κ statistic for the criterion validity ranged from 0.009 to 0.106 and was not statistically significant ($p>0.05$). Correlations ranged from $r_s = 0.385$ to 0.545 and all values were statistically significant ($p<0.05$).
CONCLUSION: κ statistic of less than 0.5 for all inter-rater reliabilities indicates the Naranjo criteria is fair, at best for the acute care setting. Intra-rater reliability for was good to excellent for all raters. Naranjo criteria had a moderate to substantial correlation with expert opinion. Overall, it appears the Naranjo criteria needs modification for use in the ICU to improve inter-rater reliability and criterion validity.

7. Use of drug metabolic pathways to predict clinically significant drug interactions: development of a simple tool for practitioners. *John R. Horn, Pharm.D.*, Philip D. Hansten, Pharm.D.; University of Washington, Seattle, WA.

PURPOSE: To develop a tool that can be used to make accurate predictions of drug-drug interactions including those that have not been identified in drug labeling or standard drug interaction reference texts.
METHODS: A database containing over 11,000 drug interaction articles was searched for references containing information on specific drug metabolic pathways (i.e., cytochrome P450s) and P-glycoprotein. In addition, articles containing data on metabolic pathways inhibited or induced (including P-glycoprotein) were identified. Only data derived from human in vivo data was included. Just over 5500 articles met the search criteria and data from over 250 drugs was noted. After discarding unused or uncommon drugs, about 220 drugs were included.
RESULTS: For each drug, the enzyme(s) responsible for its metabolism is noted, as is the drug's capability to inhibit or induce a P450 enzyme(s) or P-glycoprotein. To determine if two drugs are likely to interact, one simply compares the CYP enzyme responsible for one drug's metabolism with the enzyme(s) inhibited or induced by the second drug. For example, if a drug that is a substrate for CYP3A4 is administered with an inhibitor of CYP3A4, one can assume a reduction in the clearance of the CYP3A4 substrate will occur. The table contains 109 drugs that are known to be substrates of CYP3A4 and 25 drugs that inhibit CYP3A4. There are 2725 possible interactions between the CYP3A4 substrates and inhibitors. Only a minority of these interactions have been studied or reported.
CONCLUSIONS: Metabolic drug interactions can be easily predicted and when combined with assessment of patient risk factors, potential patient harm can be prevented.

8E. Paroxetine-induced hyponatremia in older adults: a 12-week prospective study. *Tanya J. Fabian, Pharm.D.*, Janet A. Amico, M.D., Patricia D. Kroboth, Ph.D., Benoit H. Mulsant, M.D., Sharon E. Corey, Ph.D., Amy E. Begley, M.A., Salem G. Bensasi, B.S., Elizabeth Weber, R.N., C.N.P., Mary Amanda Dew, Ph.D., Charles F. Reynolds, III, M.D., Bruce G. Pollock, M.D., Ph.D.; University of Pittsburgh; VA Pittsburgh Health System, Pittsburgh, PA.

Presented at the 42nd Annual Meeting of the New clinical Drug Evaluation Unit, Boca Raton, Florida, June 2002.

9. Liver transplantation for clarithromycin-induced subfulminant hepatic failure. *Shi-Hui Pan, Pharm.D., FCCP*, Sergio E. Rojter, M.D., David Schulman, M.D., Allen L. Hoffman, M.D., Hector C. Ramos, M.D., Richard R. Lopez, Jr., M.D.; St. Vincent Medical Center, Los Angeles, CA.

INTRODUCTION: Clarithromycin, a macrolide antibiotic, is frequently prescribed for upper respiratory tract infections and *Helicobacter pylori* induced duodenal ulcer. The common side-effects of clarithromycin are mild and transient with < 1% of abnormal liver function tests reported. In rare instances hepatic necrosis has been reported in association with macrolide antibiotics.
CASE REPORT: A previously healthy 72-year-old gentleman completed a 7-day course of clarithromycin (500 mg twice daily) and a 16-day course prednisone for an upper respiratory tract infection. The patient denied taking acetaminophen or other potentially hepatotoxic medications. Six weeks later, he developed abdominal discomfort, nausea, weakness and jaundice. The laboratory revealed: SGOT 355 U/L, SGPT 961 U/L, bilirubin 17.1 mg/dl, albumin 1.7 g/dl, protime 15.2 seconds (INR 1.54). Alkaline phosphate and complete blood counts were unremarkable. Due to progressive symptoms and hepatic failure, he was referred for possible liver transplantation. On evaluation, serologies for hepatitis A, B, and C, CMV, and EBV were negative. Blood cultures, endoscopic findings, and imaging studies were unremarkable. Despite supportive care in the hospital, the patient's condition deteriorated with worsening encephalopathy, coagulopathy, rising bilirubin, and pruritus. He underwent urgent liver transplantation and recovered uneventfully. The explanted liver revealed massive hepatic necrosis compatible with drug-induced hepatotoxicity. To avoid the potential cross hypersensitivity between clarithromycin and tacrolimus (a macrolide immunosuppressant), he was placed on cyclosporine based immunosuppression. The patient is now 24 months status post liver transplantation with normal liver function.
CONCLUSION: We believe this patient's hepatic failure was due to an idiosyncratic reaction from clarithromycin and that symptoms were delayed as a result of concomitant therapy with corticosteroids. Macrolide-induced idiosyncratic hepatotoxicity is rare but severe, and clinicians should be aware of this potential adverse effect. Timely referral to a transplant center may be warranted. In addition, the potential cross hypersensitivity between macrolide antibiotics and immunosuppressants (such as tacrolimus or sirolimus) should be avoided.

10. Role of pharmacists in improving provider recognition of drug interactions. *Pamela S. Belperio, Pharm.D., BCPS*, Peter A. Glassman, M.B.B.S., M.Sc., Barbara Simon, M.A., Andrew Lanto, M.A.; VA HSR&D Center of Excellence for the Study of Healthcare Provider Behavior; VA Greater Los Angeles Healthcare System, Los Angeles, CA.

PURPOSE: To assess provider perceptions of the pharmacists' role, including increasing provider awareness of drug interactions, in the era of physician order entry (POE) with automated drug alerts (ADAs).
METHODS: A cross-sectional survey conducted from October-December 2000 of 263 eligible providers at a large, multi-facility VA healthcare system utilizing POE with imbedded ADAs. Questions assessed knowledge of 21 possible drug and disease-state interactions, perceptions about the importance of pharmacists= tasks and experiences with ADAs (18 items).
RESULTS: Response rate was 64% (168/263). Providers recognized a median of 49% (range 11%-64%) of 10 drug interactions and 55% (range 24%-87%) of 11 drug-disease interactions. Recognition of severe/life-threatening interactions was 53%. Internists and younger providers recognized more interactions than non-medical specialists ($p<0.001$) as did those with more clinic days ($p=0.021$). There was general agreement about the value of pharmacist tasks: processing/filling prescriptions 98%, warning about drug interactions 93%, patient counseling 90%, multidisciplinary team participation 83%, ADE surveillance 82%, optimizing/managing therapy 81%. Although providers are receptive to receiving ADAs, feel ADAs improve confidence in recognizing interactions (98%), and improve safety (55%); only 4% would change therapy based on an ADA compared to 54% who felt more inclined to change medications based on pharmacist recommendations. ADA barriers included non-relevant alerts (55%) and system slowdowns (44%).
CONSLUSIONS: Providers need methods to improve their ability to recognize drug interactions. While clinicians favor ADA systems as one means to this end, they agree that more relevant information about interactions is needed. ADAs do not substitute for pharmacy services, which remain valued resources to providers and may significantly contribute to increasing provider recognition of interactions.

11. Recurring chemotherapy-associated alopecia areata: case report and review of the literature. *Susannah E. Motl, Pharm.D.*, Christopher Fausel, Pharm.D., BCPS, BCOP; University of Tennessee Health Science Center, Memphis, TN; Indiana University Hospital, Indianapolis, IN.

OBJECTIVE: To report a case of recurring partial alopecia areata resulting from chemotherapy.
CASE SUMMARY: A 52-year-old woman with stage IIIC ovarian cancer and stage I uterine cancer presents with recurring alopecia areata of her eyebrows, eyelashes, arms, legs, and pubic hair beginning five months post-cessation of paclitaxel and carboplatin chemotherapy. Alopecia areata universalis occurred three weeks after initiation of chemotherapy and regrowth normalized three months post-termination of therapy. In December 2001, the patient experienced a partial loss of eyebrows, eyelashes, and axilla hair, and total loss of leg hair. A second cycle of hair loss occurred in mid-February 2002 affecting eyebrows and eyelashes. In May 2002, the patient again observed partial loss of eyebrow and eyelash hair, along with diffuse loss of arm and pubic hair.
DISCUSSION: Alopecia is a well-recognized adverse event of chemotherapy. Cyclical alopecia areata of this pattern has not previously been reported in a cancer patient. The underlying cause of this disease is investigated. Differential diagnoses include emotional stress, hormonal disorders, alopecia neoplastica, and medication-induced hair loss. Based on the patient's previous history of hair loss provoked by medications, the recurring alopecia areata is thought to be a delayed chemotherapeutic effect. The authors hypothesize an

autoimmune reaction resulting in attack of hair follicles, as a result of chemical alteration from chemotherapy.
CONCLUSION: Oncology health-care practitioners need to evaluate unique, clinical presentations of alopecia for underlying pathology. We report an interesting case of cyclic alopecia areata of a cancer survivor potentially related to autoimmune changes instigated by chemotherapy.

12. Evaluation of the interaction between warfarin and ginkgo biloba extract. Chia-Feng Lai, M.S., Chia-Chun Chang, B.S., Chia-Hung Fu, B.S., Chi-Ming Chen, Ph.D., *Hsiang-Yin Chen, M.S., Pharm.D.*; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: Six bleeding cases have been reported with the use of ginkgo biloba extract (EGb 761), and one was linked to concurrent use of warfarin. The objective of the study was to evaluate the effect of EGb 761, a standardized ginkgo biloba extract, on warfarin and coagulation function.
METHODS: To recognize the influence of EGb 761 on pharmacokinetics and pharmacodynamics of warfarin, changes in warfarin plasma concentration and prothrombin time (PT) after coadministration with EGb 761 was studied in a Sprague Dawley rat model. Clinical cases with concurrent use of two drugs were also retrospectively reviewed to evaluate the relationship between EGb 761 and international normalized ratio (INR). Changes of coagulation parameters, including platelet counts, INR, bleeding time, clotting time, was determinated in twelve healthy volunteers taking EGb 761 120 mg once daily for 28 days.
RESULTS: A significant decrease in the area under plasma concentration-time curves (AUC) from 22.54 ± 2.67 to 17.27 ± 1.64 μg•hr/ml, was detected with coadministration of EGb 761 under a multiple dosing design. ($p=0.002$) Similarly, maximal PT and area under the PT versus time curve were significantly reduced with EGb 761 treatment group. ($p<0.01$) There was no significant change in INR after adding EGb 761 in 21 clinical cases. ($p=0.551$) No clinically significant change in coagulation parameters was observed when finishing the regimen.
CONCLUSIONS: No clinically significant influence of EGb 761 on warfarin was found on clinical cases and healthy volunteers. As the animal results of decreased pharmacokinetic and pharmacodynamic effects of warfarin, careful monitoring of PT was recommended with concurrent use of EGb 761 and warfarin.

13. Incidence of infusion-related reactions with infliximab: effect of pretreatment. *Anthony T. Gerlach, Pharm.D.,* Sondra J. Sierawski, R.Ph., Helen Hollis, R.N.; Ohio State University Medical Center, Columbus, OH.

INTRODUCTION: Infliximab is a monoclonal antibody that causes infusion related reactions in up to 17% of patients. Volunteer reporting of adverse drug reactions demonstrated that infliximab was associated with a high incidence of infusion related reactions at our institution. The purpose of this study was to prospectively monitor the use of infliximab for safety.
METHODS: Data was prospectively collected for any patient who received infliximab from August 2001 to February 2002. Data collected included demographics, indication, dosing acetaminophen (APAP) and diphenhydramine pretreatment, and adverse effects. Infusion related ADRs were defined as headache, fever, chills, respiratory symptoms (tachypnea and dyspnea), skin reactions, visual disturbances, nausea, hypertension, and hypotension. Statistical analysis was preformed by Fisher's exact test for nominal data and independent t test for continuous data.
RESULTS: Forty-one patients who received 62 doses of infliximab were evaluated. Pretreatment with (APAP) and diphenhydramine was given in 58% (36/62) of the cases, and the overall incidence of infusion related reactions was 18% (11/62).

	Pretreatment N=36	No Pretreatment N=26	P value
Average Age	52 (± 14.6)	36.5 (± 16.7)	< 0.05
% Female	83	65	NS
Indication			< 0.05
Crohn's Disease	4	16	
Rheumatoid Arthritis	32	9	
Average Dose	266 mg (± 59)	322 mg (± 134)	NS
ADR	2	9	< 0.05

NS=Non-significant

CONCLUSIONS: Patients with rheumatoid arthritis are more likely to be pretreated for infusion related ADRs, and pretreatment with APAP and diphenhydramine is associated with statistically significant fewer infusion related ADRs. Targets for education and improvement have been identified.

14. The epidemiology of grapefruit juice-drug interactions: a study to characterize the types and pattern of grapefruit juice consumption among Americans. *Mandy Walker, Pharm.D.,* Julie Kim, Mira Loh-Trivedi, Lingtak-Neander Chan, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Existing grapefruit juice (GFJ)-drug interaction studies have been conducted using double-strength, frozen concentrates of white grapefruits. The purpose of this study is to 1) characterize the types and pattern of GFJ consumption by the public; 2) assess the frequency of the occurrence of GFJ-drug interactions.
METHODS: A random sample of 225 people in the Chicago area was interviewed. Data collection includes demographics, medical history, current medications, types, amount and frequency of grapefruit products consumed, and subjects' knowledge in GFJ-drug interactions.
RESULTS: Of the 225 participants; 171 (76%) reported drinking GFJ, while 133 (59%) reported eating grapefruit at least once in their lifetime. GFJ consumption was most popular in the second, fifth, and sixth decade of life. Red or ruby-pink GFJ was consumed by the majority (70%) and less than 1% consumed frozen concentrates. Most GFJ consumers (53%) had less than 12 consumptions yearly. One hundred twenty-two respondents (54%) were taking prescription drugs and consuming GFJ concomitantly. Of these 122 respondents, 31 (25%) were taking known interacting medications. The most common chronic disease in these 31 respondents was cardiovascular diseases (51%), followed by hypercholesterolemia (32%). Forty-eight percent of them were unaware of GFJ-drug interactions.
CONCLUSIONS: The overall incidence of GFJ-drug interaction is 25% among people taking prescription medications. However, the design of the existing GFJ-drug interaction studies does not reflect the pattern of GFJ consumption by the public. Since red grapefruit contains less inhibitory components of CYP3A4, the magnitude of this interaction might have been exaggerated by the published studies.

15E. Venlafaxine-induced ecchymosis. *Maha Sadek, B.S., Pharm.D.,* Henry Cohen, B.S., M.S., Pharm.D., Nancy Talavera, M.D.; Kingsbrook Jewish Medical Center; Long Island University, Brooklyn, NY.

Presented at the Midyear Meeting of the American Society of Health-System Pharmacists, New Orleans, LA, December 2-6, 2001.

Analgesia

16. Pain assessment and pharmacotherapy in terminal disease: attitudes, knowledge, and practices of hospice nurses. *Kenneth C. Jackson, II, Pharm.D.,* D'Neal Riney Harle, Pharm.D. candidate; Texas Tech University Health Sciences Center, Lubbock, TX.

PURPOSE: Patients with terminal illness are often referred to hospices, where nurses treat pain and other symptoms. This project evaluates the attitudes and knowledge of pain pharmacotherapy in hospice nurses, and derives data on actual pain assessment and management.
METHODS: Questions were administered to assess attitudes and knowledge regarding pain in a group of hospice nurses (n=11). The content was derived from current standards and has been validated by recognized experts. Charts were reviewed (n=25) to evaluate pain assessment and management.
RESULTS: Nurses generally had six or more years experience in hospice (81%). Most (91%) felt comfortable/very comfortable with pain assessment, but many (73%) were uncomfortable/very uncomfortable with equianalgesic conversions. Weaknesses identified by questionnaire included therapeutics, adverse effects, dosing/titration, and addiction. Strengths included physiology, perception, assessment, and special populations. On admission 96% of charts revealed a pain assessment, only 72% using a validated tool. Drug-related problems were common (96% of charts), and included excessive acetaminophen use, inappropriate propoxyphene use, potential adverse drug reaction, and therapeutic duplications. Others included inappropriate dosing, inappropriate selection, and lack of prophylactic bowel regimens. Overall, 80% of charts revealed inappropriate assessment and management of pain.
CONCLUSION: These results indicate a need for hospice nurses to pursue an improved understanding of the assessment and management of pain. Issues related to pain assessment and pharmacotherapy were common, confirming the need for improved knowledge about pain. This data provides a platform for clinically trained pharmacists to explore potential roles as hospice consultants, ranging from staff development to patient management.

Cardiology

17. Questioning a class effect: does angiotensin-converting enzyme inhibitor tissue penetration influence markers of myocardial reinfarction risk? *James P. Tsikouris, Pharm.D.,* Jose A. Suarez, M.D., Martin Ziska, B.S., Gary E. Meyerrose, M.D.; Texas Tech University, Lubbock, TX.

There is a common belief in a class effect amongst ACE inhibitors (ACEI). This is unsubstantiated for acute myocardial infarction (AMI). Because vascular tissue is a primary source of the endogenous fibrinolytic, tissue plasminogen activator (t-PA) and it's inhibitor plasminogen activator inhibitor-1 (PAI-1), and ACE inhibition in vascular tissue favorably influences the fibrinolytic system, we hypothesized that a high-tissue penetrating ACEI would provide more favorable reduction in PAI-1 and increase in t-PA after AMI compared to a low-tissue penetrating ACEI.
METHODS: In a randomized open-label trial, patients received a high-tissue penetrator (Quinapril) or low-tissue penetrator (Enalapril) for 14 days following AMI. PAI-1 and t-PA antigen (ng/ml) were measured at baseline, then 12 hours, and Day 1, Day 2, Day 3, Day 7, Day 14 after drug initiation.
RESULTS: There was no difference in baseline PAI-1 or t-PA antigen with

Quinapril (n=13) and Enalapril (n=14) patients (PAI-1: 29.7 ± 13.1 vs. 30.5 ± 11.3; and t-PA: 15.9 ± 5.7 vs. 17.2 ± 7.5, respectively). There were no differences in t-PA levels between agents during the 14-day treatment. PAI-1 was lower with Quinapril versus Enalapril at each time point starting with Day 1 (Day 1: 26.7 ± 15.9 vs. 34.2 ± 19.5; Day 2: 18.8 ± 13.3 vs. 23.2 ± 14.5; Day 7: 22.9 ± 10.3 vs. 27.7 ± 12.9; Day 14: 22.1 ± 12.6 vs. 26.1 ± 11.8), being significantly lower on Day 3 (18.1 ± 10 vs. 26.6 ± 8.9, respectively, p=0.037).
CONCLUSION: This first investigation of ACEI tissue penetrating influence on markers of reinfarction, suggests an earlier benefit with a more highly tissue penetrating ACEI, warranting further investigation.

18. Clinical experience with ultra low-dose amiodarone (100 mg/day). *Maria G. Tanzi, Pharm.D.*, Marieke D. Schoen, Pharm.D., BCPS, Jerry L. Bauman, Pharm.D., BCPS, FCCP; University of Illinois at Chicago, Chicago, IL.

PURPOSE: In an attempt to reduce toxicity while maintaining effectiveness, many centers routinely decrease patients (pts) to 100 mg/day of amiodarone (amio) despite the lack of evidence for this dosage. Therefore, we report our experience with ultra low-dose amio (100 mg/day) compared to standard low-dose amio (200 mg/day) in the prevention of supraventricular and ventricular arrhythmias.
METHODS: We screened our database of 204 patients enrolled in a collaboratively managed amiodarone clinic for those being treated with amio 100 mg/day for at least 6 months. A control group was established by randomly selecting patients on amio 200 mg/day in a 2:1 (200 mg:100 mg) ratio. Effectiveness was defined as the prevention of documented recurrence of the pts tachycardia.
RESULTS: Comparisons were made between 25 pts who fulfilled the criteria for inclusion (100 mg/day) and 50 controls (200 mg/day). There were no significant differences in age, sex, and indications for therapy between the 2 groups. At 21.2 ± 17.5 months of therapy, recurrence of the pts tachycardia occurred in 7/25 (28%) on 100 mg/day compared to 10/50 (20%) on 200 mg/day for 18.4 ± 14.3 months of therapy (p=NS). Kaplen-Meir curves of the 2 groups were not significantly different (p=NS). Drug discontinuation was similar between the 100 mg/day 5/25 (20%) and 200 mg/day 11/50 (22%) groups (p=NS).
CONCLUSION: In patients being successfully maintained on 200 mg/day amio, the dosage can be reduced to 100 mg/day without a significant loss in effectiveness.

19. The effect of oral anticoagulant therapy on event rates in patients after acute coronary syndromes: a systematic review. *Brian G. Katona, Pharm.D.*, David L. Larimer, R.Ph., Jay C. Horrow, M.D., M.S., Gary Peters, M.D.; AstraZeneca, Wilmington, DE.

PURPOSE: Critically analyze and update the effectiveness of oral anti-coagulant (OA) therapy in patients with acute coronary syndromes (ACS).
METHODS: MEDLINE, EMBASE, and Current Contents were searched between 1998 and 2002. All randomized, controlled trials were identified and placed in the categories of low (INR < 2.0), moderate (INR 2-3), or high intensity anticoagulation (INR > 3); with or without concomitant aspirin use. We then updated the meta-analysis of Anand and Yusuf (JAMA 1999; 282: 2058-67), using identical statistical methods, comparing the effectiveness of OA therapy on the composite endpoint of death, myocardial infarction, and stroke versus major bleeding.
RESULTS: 5 major randomized clinical trials, which enrolled a total of 13,704 patients, were added to the 12,396 patients of Anand, et al.

Level of Intensity	Events OA	Events Control	P value	Odds Ratio
Moderate & High vs. ASA	281/2083 (13.5%)	339/2074 (16.3%)	0.0078	0.79 (.67-.94)
Moderate or High + ASA vs. ASA	361/3785 (9.5%)	474/3797 (12.5%)	< 0.0001	0.73 (.63-.85)
Low + ASA vs. ASA	1232/6733 (18.3%)	1267/6761 (18.7%)	0.51	0.97 (.88-1.1)

(continued)

Level of Intensity	Major Bleeding OA	Major Bleeding ASA	P value	Odds Ratio
Moderate & High vs. ASA	101/2083 (4.8%)	55/2074 (2.7%)	0.0002	1.9 (1.2-2.6)*
Moderate or High + ASA vs. ASA	178/3785 (4.7%)	39/3797 (1%)	<0.0001	2.3 (1.6-3.4)
Low + ASA vs. ASA	184/6733 (4.6%)	128/6761 (1.9%)	0.0012	1.5 (1.2-1.8)

*Failed test of homogeneity

CONCLUSIONS: With or without concomitant aspirin, moderate or high dose OA, but not low dose OA prevents death, recurrent myocardial infarction, and stroke better than aspirin alone in patients with ACS. All OA-containing regimens confer a higher major bleeding risk than ASA alone.

20. Cost-savings associated with a decreased need for potassium supplementation in heart failure patients on spironolactone. *Amber L. Beitelshees, Pharm.D.*, Jerry L. Bauman, Pharm.D., FCCP, Mary Ross Southworth, Pharm.D., Robert J. DiDomenico, Pharm.D., Stephanie H. Dunlap, M.D., Lucy A. Fashingbauer, B.S., Larisa M. Humma, Pharm.D., BCPS; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Spironolactone has been shown to improve heart failure outcomes. We sought to determine whether spironolactone use in heart failure was associated with a cost savings secondary to a decreased need for potassium (K) supplementation.
METHODS: We reviewed clinic records for patients with severe heart failure receiving standard therapy including an ACE inhibitor and compared patient costs of K ± spironolactone (1) between patients on and not on spironolactone and (2) before and after spironolactone initiation specifically for those taking spironolactone.
RESULTS: Of 94 patients identified, 44 were on chronic spironolactone therapy (mean ± SD dose: 27 ± 10 mg/day). Eighteen (41%) spironolactone-treated patients and 31 (62%) non-treated patients required K to maintain serum K within normal limits (p<0.05); median (range) K dose was 40 (20-180) mEq/day with and 40 (16-80) mEq/day without spironolactone. Median (range) monthly cost of K ± spironolactone was $10.70 (5.37-238.35) with and $50.60 (5.99-101.16) without spironolactone (p<0.01). Among 28 spironolactone-treated patients with available data, 18 (64%) required K before and 15 (54%) required K after spironolactone initiation. Median (range) monthly cost of K ± spironolactone was $50.60 (12.65-101.16) before and $33.30 (5.37-238.35) after spironolactone initiation (p=NS). Further analysis revealed possible racial differences in K requirements with spironolactone; median (range) K dose was 20 (14.25-112) mEq/day in Caucasians and 40 (20-180) mEq/day in African Americans (p=0.06).
CONCLUSIONS: Heart failure patients treated with spironolactone may derive some savings associated with reduced K requirements. Our data suggest that there may be racial differences in K requirements with spironolactone and thus, cost savings may also differ by race.

21. Sustained impact of a pharmacist-based lipid optimization program for chronic heart disease patients. Robert J. Straka, Pharm.D., FCCP, *Kelly Z. Hadsall, Pharm.D.*, Ali Toumadj, Pharm.D. candidate, Susan Cooper, R.Ph., M.S., James Smith, M.D.; University of Minnesota, Minneapolis, MN; HealthPartners, Bloomington, MN.

BACKGROUND: Intensive programs to optimize the management of hypercholesterolemia have demonstrated effectiveness in achieving target LDL-C (<100mg/dL) in chronic heart disease (CHD) patients. We previously reported results of a 28-week, multi-clinic, controlled study, comparing a pharmacist based model (intervention group) to usual care (control group). The ACTION Trial (*Pharmacotherapy* 2000;20:1234) documented a 35.6mg/dL (27%) reduction in the average LDL-C in the intervention group (n=150) compared to a 6.7 mg/dL (4.6%) drop in the control arm (n=331), (p<0.001) from mean (SD) baseline values of 131mg/dL (± 28) and 131mg/dL (± 26) respectively (p<0.001). The need to follow-up intervention group participants has resource related implications.
PURPOSE: To evaluate the need for follow-up of patients post completion of an intensive program aimed at optimizing management of hyper-cholesterolemia.
METHODS: Electronic records were used to retrieve the last available fasting lipid panels up to 17.5 months (out to 7/30/2001) following the interventions of the ACTION Trial (ending 2/15/2000). Unpaired t-test and Chi Squared analysis were used for between group comparisons for continuous and dichotomous data respectively.
RESULTS:

	Control Group (n=229) mg/dL mean (SD)	Intervention Group (n=130) mg/dL mean (SD)	Significance
LDL-C Baseline	130 (26)	130 (26)	NS
LDL-C Final*	124 (38)	95 (19)	p<0.001
LDL-C Follow-up**	111 (33)	95 (23)	p<0.001
Δ LDL-C (final to Follow-up)	-11.2 (32)	-0.3 (21)	p<0.001
N (%) at goal LDL-C	96 (42)	84 (65)	p<0.001
Mean (SD) Follow-up* (days)	476 (165)	440(144)	NS

*End of ACTION Trial; **from end of ACTION Trial (and all interventions) until last available lipid panel

CONCLUSION: Our pharmacy based collaborative approach to optimize lipid management in CHD patients appears to have sustained its effect in the absence of continued effort. Progress within the control group suggests improvements in the clinic's management of hypercholesterolemia relative to baseline. Evidence of sustained effects contribute to the long-term value of initial investments of effort for those not at goal LDL-C.

22. The effects of intravenous levofloxacin on the electrocardiographic QT interval. *Maha Sadek, B.S., Pharm.D.*, Ravindra Bharadwaj, M.D., Henry Cohen, B.S., M.S., Pharm.D., CGP, BCPS, Abdul Malik, M.D., Liz Ramos, B.S., M.S., Pharm.D., Rizwanullah Hameed, M.D., Liyaquat Hayat, M.D., Prabir Banik, M.D., Imran Ahmed, M.D., Devang Lodhavia, M.D.; Kingsbrook Jewish Medical Center; Long Island University, Brooklyn, NY.

PURPOSE: To determined if levofloxacin induces electrocardiographic (ECG) QT interval prolongation.
METHODS: This was a prospective, non-randomized study of 50 adult patients (54% females) (mean age 72 ± 14) admitted from the emergency department that were prescribed intravenous levofloxacin. All patients received at baseline (T_1) and after the third dose of levofloxacin (T_2) a

physical exam, serum chemistry panel and an ECG. Patients receiving any QT-prolonging drugs or had congenital long-QT-syndrome were excluded. The QTc interval was calculated using Bazett's formula. Student's paired t test was utilized to compare the T_1 and T_2 mean QTc intervals.
RESULTS: The mean QTc at T_1 was 421 ± 57 msec (range 266-694), and at T_2 was 439 ± 63.36 msec (range 338–682), (p=0.026). Patients who received the appropriate levofloxacin dose based on manufacturers guidelines (40%) had a T_1 and T_2 mean QTc of 415 ± 37 msec, and 433 ± 44 msec, respectively. Patients receiving double the levofloxacin dose (60%), had a T_1 and T_2 mean QTc of 424 ± 67 msec, and 443 ± 74 msec, respectively. Nine patients had a T_1 and T_2 mean QTc moderately increase from < 450 msec (393 ± 52) to ≥ 450 msec (500 ± 22). When available, serum electrolytes were normal, calcium (n=47), potassium (n=49), and magnesium (n=19). None of our patients developed signs or symptoms of dysrhythmias.
CONCLUSION: Intravenous levofloxacin significantly prolonged the QTc interval by 18 ± 57 msec in our patients.

23. The effects of renal failure and hypoalbuminemia on the protein binding of cerivastatin in hemodialysis patients. Rita Neilan, Pharm.D., *Henry Cohen, M.S., Pharm.D.*, Robert V. DiGregorio, Pharm.D., Sonia Borra, M.D., Joseph P. Reilly, Pharm.D., Roopali Sharma, Pharm.D.; Kingsbrook Jewish Medical Center; Long Island University, Brooklyn, NY.

PURPOSE: Cerivastatin is approximately 99-99.5% protein bound primarily to serum albumin, therefore, under normal conditions, the fraction unbound (f_u) is ≤1%. The objective of this prospective, open-label study is to evaluate the effects of renal failure and hypoalbuminemia on the protein binding of single dose cerivastatin.
METHODS: Eighteen stable adult hypoalbuminemic patients receiving hemodialysis were randomized to receive a single dose of cerivastatin 0.2 mg (n=9) or 0.4 mg (n=9) two hours before hemodialysis. Cerivastatin total and unbound concentrations pre- and post-hemodialysis were determined by HPLC.
RESULTS: The mean albumin level and Cl_{cr} for both groups was 3.16 ± 0.40 mg/dL, and 11.45 ± 5.30 mL/min, respectively. The mean pre-hemodialysis and post-hemodialysis BUN for both groups was 59.3 mg/dL and 16.7 mg/dL, respectively. The mean f_u cerivastatin pre-hemodialysis was 2.12% (range 1.17%-2.95%). The mean f_u cerivastatin post-hemodialysis was 1.62% (range 1.05%-2.81%), remaining above normal. The correlation obtained with f_u cerivastatin utilizing Pearsons' correlation coefficient, was greatest (fair to good) with albumin, and least (little to fair) with Cl_{cr}. However, the correlations were not statistically significant (p>0.05), plausibly due to the small sample size. No adverse events occurred.
CONCLUSION: In 18 hemodialysis patients, the cerivastatin f_u was found to be 2–3 times the normal range in all samples assayed. Since most statins are highly protein bound, an increased risk of adverse effects in renal failure patients with hypoalbuminemia is plausible. However, this was a single dose study, a multiple dose study is necessary to corroborate our findings.

24. Impact of an intravenous and oral amiodarone regimen in the post-open heart surgery Atrial Fibrillation Suppression Trial II. *C. Michael White, Pharm.D.*, James S. Kalus, Pharm.D., Michael F. Caron, Pharm.D., Jessica Song, Pharm.D., Heidi Rose, R.N., James P. Tsikouris, Pharm.D., Jeffrey Kluger, M.D.; University of Connecticut, Storrs, CT; Hartford Hospital, Hartford, CT; University of the Pacific, Stockton, CA; Texas Tech University, Lubbock, TX.

PURPOSE: In the Atrial Fibrillation Suppression Trial (AFIST I), we found that adding prophylactic oral amiodarone to patients receiving β-blockers could reduce post-open heart surgery (OHS) atrial fibrillation (AF) and symptomatic AF. Amiodarone was given either as 7 g over 10 days (5 days before and 5 days post-OHS) or 6 g over 6 days (1 day before and 5 days post-OHS). The 10-day regimen had better efficacy than the 6-day regimen but was technically more difficult to administer. In AFIST II, we evaluated whether an intravenous (IV) and oral amiodarone regimen delivering the equivalent of 7 g of oral amiodarone during the post-OHS time period only could suppress AF and symptomatic AF.
METHODS: Patients (n=160, age 65.8 ± 8.7 years, 76% male, 21.3% valve surgery, 81.9% post-OHS β-blocker use) were randomized to amiodarone (1.05g over 24 hours IV on day of surgery and 4.8 g orally over post-OHS days 1-4 (400 mg TID) or matching placebo. No significant demographic differences were found between groups. The incidence of AF (any AF lasting > 5 min) and symptomatic AF were evaluated.
RESULTS: Amiodarone reduced the risk of AF (22.1% vs. 38.6%; p=0.037) and symptomatic AF (6.5% vs. 20.5%; p=0.019) by 42.7% and 68.3% versus placebo, respectively.
CONCLUSIONS: Amiodarone given intravenously over 24 hours on the day of surgery and then orally on postoperative days 1-4 significantly reduces the risk of post-OHS atrial fibrillation and symptomatic atrial fibrillation. Thus, it provides similar efficacy to the all-oral amiodarone dosing strategy in AFIST I but may be easier to implement for health-systems.

25. What is the effect of amiodarone on P-wave variables in cardiac surgery patients? *James S. Kalus, Pharm.D.*, Michael F. Caron, Pharm.D., Xinhcun Liu, B.S., Heidi L. Rose, R.N., Jeffrey Kluger, M.D., C. Michael White, Pharm.D.; Hartford Hospital, Hartford, CT; University of Connecticut, Storrs, CT.

PURPOSE: The P-wave represents atrial depolarization on the 12-lead electrocardiogram. P-wave duration measurements in patients with paroxysmal atrial fibrillation are longer than measurements in healthy controls, suggesting delayed atrial depolarization in patients with paroxysmal atrial fibrillation. Atrial fibrillation most commonly occurs after cardiac surgery on postoperative days 2 and 3 and prophylactic amiodarone administered postoperatively may decrease the occurrence of this common surgical complication. We evaluated the effects of amiodarone on P-wave duration in order to define a mechanism for its effect on the development of postoperative atrial fibrillation.
METHODS: Patients (n = 160, 65.8 plus/minus 8.7 years, 76% male, 21.3% valve surgery) were randomized to amiodarone or placebo for 5 days (1 gram intravenously on the day of surgery and 1200 mg orally on postoperative days 1-4). 12-lead electrocardiograms were taken on the day of surgery through postoperative day 4 and P-waves were measured by a blinded investigator.
RESULTS: On postoperative day 2, average and minimum P-wave duration among patients receiving amiodarone were reduced by 10.3% (p=0.009) and 24.3% (p=0.0004), respectively, compared to the placebo group. On postoperative day 3, there was a 22% decrease in minimum P-wave duration (p=0.0007).
CONCLUSION: Amiodarone shortened P-wave duration on the postoperative days when atrial fibrillation is most likely to occur. These results suggest that delayed atrial depolarization in post-cardiac surgery patients is attenuated by amiodarone. This effect may explain the role of amiodarone in reducing the occurrence of postoperative atrial fibrillation.

26E. Regional isoproterenol increases defibrillation energy requirements. *J. Jason Sims, Pharm.D.*, Kell L. Schoff, B.S., Jennifer M. Loeb, B.S., Nicholas A. Wiegert, B.S.; University of Wisconsin, Madison, WI.

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27. Evaluation of perioperative β-blocker use for the prevention of cardiovascular complications in elective, noncardiac surgery. *Bradi L. Frei, Pharm.D.*, Chris R. Frei, Pharm.D., Robert L. Talbert, Pharm.D., BCPS; University of Texas at Austin, Austin, TX; University of Texas Health Science Center, San Antonio, TX.

PURPOSE: To evaluate perioperative β-blocker use in patients at risk for post-surgery cardiovascular complications undergoing elective, noncardiac surgery.
METHODS: We conducted a retrospective, cohort study, using medical record data, of adult patients undergoing major noncardiac surgery with general anesthesia at a university teaching hospital during a 6-month period in 1999. Patients with two or more cardiac risk factors or with documented coronary artery disease were classified as high risk and considered eligible for perioperative treatment with a β-blocker unless contraindications to its use were present. Cardiac risk factors were ≥ 65 years, hypertension, smoking, total cholesterol ≥ 240 mg/dl, and diabetes mellitus. Death from all causes was determined for all 96 patients using the Social Security Death Index.
RESULTS: Of the 208 charts reviewed, 96 (46%) patients were ideal candidates for administration of perioperative β-blockers. Of these 96 patients, 28 (29%) received a β-blocker perioperatively at some time. Of these 28 patients, 15 (54%) were receiving β-blockers prior to hospital admission. Death from all causes was higher in patients who received β-blockers (21%) compares to those who did not receive on (7%). However, β-blocker patients also had a higher incidence of CAD (35% vs. 13%), DM (67% vs. 60%), and smokers (43% vs. 32%) compared to those not receiving β-blockers.
CONCLUSIONS: β-Blockers are substantially underutilized at our institution despite guidelines recommending their use in high-risk patients. β-blockers were more likely to be used in patients with CAD, which could account for the increased mortality rate among those patients receiving β-blockers.

28. Ibutilide is less proarrhythmic when instilled into the pericardial fluid space. *Michael R. Ujhelyi, Pharm.D.*, Kelly Z. Hadsell, Pharm.D.; Medtronic, Inc., Minneapolis, MN.

BACKGROUND: Pericardial delivery (PD) of antiarrhythmic drugs yields pericardial fluid concentrations that are 1000X greater than intravenous delivery (IV). This dosing advantage may be offset by increased proarrhythmia, although this may not be true for water soluble antiarrhythmics (i.e., ibutilide) because vascular uptake could limit ventricular tissue diffusion (Circ 2000;102:II672) and hence ventricular proarrhythmia.
METHODS: We assessed ibutilide's potential to induce sustained polymorphic ventricular tachycardia (PVT) in 9 chronic (6 weeks) AV blocked dogs that developed LV hypertrophy (heart/body weight = 0.93 ± 0.13%). Dogs were randomized to 3 sequential PD doses (1.9, 3.8 and 15 ug/kg, N=4) or 2 sequential IV doses (7.5 and 7.5 ug/kg, N=5) based upon clinical dose of 15 ug/kg. IB doses were infused for 5 minutes, followed 45 minutes later by endocardial right and left refractory period (ERP) testing, and programmed electrical stimulation (PES). This protocol was repeated with each sequential dose.

RESULTS: Incidence of spontaneous PVT, PES induced PVT with short-long-short stimuli, and death due to incessant PVT. Spontaneous PVT occurred at the lowest IV dose (7.5 ug/kg) vs. at the highest PD dose (15 ug/kg). Time to spontaneous PVT was also significantly shorter with IV vs. PD ibutilide (7.1 ± 2.2 vs. 42 ± 12 min, p<0.05). Similarly, PES induced PVT and PVT related death all occurred at lower IV versus PD doses. All IV doses caused electrical instability (PVCs and PVT) such that ERP could not be determined. For PD, the 1.9 and 3.8 ug/kg had no effect on ERP, while the 15 ug/kg PD dose prolonged LV ERP by 30-50% at cycle lengths 750-1500 (p<0.05) ms but did not affect RV ERP indicating ERP dispersion.

	Spont-PVT	PES-PVT	Death
PD baseline	0%	0%	0%
PD-1.9 ug/kg	0%	0%	0%
PD-3.8 ug/kg	0%	25%	0%
PD-15 ug/kg	50%	75%	25%
IV Baseline	0%	20%	0%
IV-7.5 ug/kg	75%	75%	20%
IV 7.5 ug/kg	100%	75%	60%

CONCLUSIONS: Pericardial ibutilide is less proarrhythmic than IV delivery even at higher doses. This suggests that pericardial ibutilide delivery has a larger ventricular proarrhythmia safety margin than intravenous ibutilide delivery.

29. Antiarrhythmic drug use during the Model 7250 Jewel AF (AF only) clinical study. *Michael R. Ujhelyi, Pharm.D.,* Jodi Koehler, M.S., Anna Lindlief, Pharm.D., David Schwartzman, M.D.; Medtronic, Inc.; Minneapolis, MN.

BACKGROUND: The Medtronic Jewel AF (model 7250) is an ICD with pacing and defibrillation therapies to terminate atrial tachyarrhythmias (AT) and VT/VF. Jewel AF may limit the use antiarrhythmic drug (AAD) usage because the device has several means to treat and/or prevent AT. The Jewel AF multicenter 'AF only' (no VT/VF) study was examined to determine AAD (Vaughan Williams class I and III) usage patterns after device implant and determine the role of hybrid device plus drug therapy for AT management.
METHODS: Enrollment required ≥ 2 symptomatic AT events 3 months pre-implant and refractory or intolerant of ≥ 1 Class I, II, III or IV AAD. Of the 144 patients, 132 had ≥ 6 months follow up. This cohort was followed for 12 ± 6 months and AAD was tabulated at implant, 3, 6, 12 and 18-months. AAD use was at investigator's discretion.
RESULTS: From the time of device implant, 103 of 132 (77%) patients used an AAD at least once during follow up, while 23% never received an AAD. At implant, 80 (60%) patients were on AAD therapy. AAD at implant consisted of amiodarone (54%) or sotalol (28%) treatment, which remained constant at 6, 12 and 18-month follow-ups. During follow up, 62 patients had no changes to AAD therapy (stable), while 70 patients had unstable AAD therapy where 23 patients started, 21 stopped, and 26 switched AAD therapy. Interestingly, the majority (96%) of the 70 patients who had an AAD change did so within the first 6 months after implant. From the 6-month follow up, nearly 40% of patients remained stable off AAD therapy. Moreover, patients that were classified as stable AAD therapy had significantly fewer device treated AT/AF episodes/week than patients who were classified as unstable AAD (0.12 range 0-6.2 vs.0.56 range 0-21.7, p<0.05). However, this difference only occurred during the 0-3 month follow up period after implant. After this time, AT/AF episodes decrease in the unstable group equaling the stable AAD group (0.08 range 0-16.1 vs. 0.09 range 0-52.5).
CONCLUSIONS: AAD therapy is unstable during the first 0-3months after Jewel AF implant. Unstable AAD therapy correlates with greater number of device treated AT/AF episodes, suggesting a hybrid therapy approach. After 6-months, approximately 40% of Jewel AF patients are managed without AAD therapy and this correlates with a lower AT/AF frequency.

30. Prevention of atrial fibrillation after open-heart surgery: an economic comparison of placebo, amiodarone, pacing and amiodarone plus pacing. Prabashni Reddy, Pharm.D., Angiliki Karapanos, Pharm.D. candidate, *James S. Kalus, Pharm.D.,* Michael F. Caron, Pharm.D., Craig I. Coleman, Charles M. White, Pharm.D.; University of Connecticut, Storrs, CT; Hartford Hospital, Hartford, CT.

PURPOSE: We recently showed, in a randomized trial, that amiodarone plus pacing significantly decreased postoperative atrial fibrillation after open-heart surgery, compared to amiodarone, pacing and placebo. The purpose of this sub-study was to compare index hospital admission and 30 day costs between the groups.
METHODS: A piggyback cost analysis of the clinical trial was conducted from a hospital perspective. The study timeframe was 30 days from day of surgery. Hospital charges and readmissions were obtained from hospital databases. Charges were converted to costs using cost-to-charge ratios. Costs were compared using analysis of variance.
RESULTS: Index hospital costs were > $20,000 in 35%, 33%, 34% and 29% of the placebo, amiodarone, pacing and amiodarone plus pacing patients, respectively (p=1.00). Costs (mean ± SD) for the index admission were $27,026 ± 30,226 in the placebo, $22,725 ± 17,661 in the amiodarone, $33,868 ± 60,309 in the pacing and $18,697 ± 8,174 in the amiodarone plus biatrial pacing groups (p=0.27). There was a trend towards a difference in the number of hospital readmissions (placebo:0.04 ± 0.20, amiodarone: 0.08 ± 0.27, pacing: 0.00 ± 0.00, amiodarone plus pacing 0.16 ± 0.44; p=0.08) although readmission costs were similar (placebo: $452 ± 2,799; amiodarone: $623 ± 2,184; pacing: $0.00 ± 0.00; amiodarone plus pacing: $1,153 ± 3,165; p=0.28). Cumulative costs (index + readmissions) at 30 days were $27,478 ± 30,191; $23,557 ± 18,146; $33,868 ± 60,309 and $20,284 ± 11,551 among placebo, amiodarone, pacing and amiodarone plus pacing patients, respectively (p=0.38).
CONCLUSIONS: Since amiodarone plus pacing is more efficacious and has similar costs to alternative therapies, this novel strategy is a cost-effective option in post-operative atrial fibrillation prevention. Larger studies should be undertaken, powered to detect cost differences between strategies to lower atrial fibrillation after open-heart surgery.

31. Cost-effectiveness of GP IIb/IIIa inhibitors in a national database of acute myocardial infarction patients. *Patrick L. McCollam, Pharm.D.,* David A. Foster, Ph.D., Jeffrey S. Riesmeyer, M.D.; Eli Lilly & Co., Indianapolis, IN; Solucient, Inc., Ann Arbor, MI.

PURPOSE: To determine cost-effectiveness (C/E) of adjunctive GPIIb/IIIa inhibitor use during percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) patients.
METHODS: Data (1/1/2000-6/30/2001) from Solucient's (Evanston, IL) national all-payer database were analyzed for any AMI patient undergoing PCI and receiving a GPIIb/IIIa inhibitor compared to non-GPIIb/IIIa recipients. Risk adjustment for mortality was performed by logistic regression using published methods to account for differences in patient and hospital characteristics using all pertinent variables contained in the data set (age, sex, diagnoses, procedures, clinical grouping, length of stay, hospital size, census division, teaching status, urban or rural setting). Incremental costs were determined by least squares regression to fit general linear models. C/E was estimated using published methods. Mortality and cost results refer to the in-hospital period.
RESULTS: Data were from 32,529 patients in 99 hospitals. C/E was calculated for abciximab since only it demonstrated a significant difference in the effectiveness measure (survival). The C/E was < $15,000 per life year gained.

	Risk-adjusted Mortality	Incremental Hospital Costs
Abciximab (n=11,816)	0.74* (0.59-0.92)	$1807† (1529-2085)
Eptifibatide (n=10,093)	0.87 (0.68-1.10)	$1147† (849-1445)
Tirofiban (n=3,700)	0.99 (0.73-1.34)	$644† (252-1036)

data are expressed as: odds ratio and (95% CI) vs. the non-GPIIb/IIIa group; *p=0.007; †p<0.0001

CONCLUSION: These recent data provide additional insight into contemporary use of GPIIb/IIIa inhibitors in AMI patients undergoing PCI in actual clinical practice. During the index hospitalization, only abciximab demonstrated a significant survival benefit vs. the non-GPIIb/IIIa group and it possessed a favorable C/E ratio.

32E. β-Adrenergic inhibition of leptin production is attenuated in obese individuals. *John M. Dopp, Pharm.D.,* Alexei V. Agapitov, M.D., William G. Haynes, M.D., Christine A. Sinkey, R.N., Virend K. Somers, M.D., Bradley G. Phillips, Pharm.D.; University of Iowa, Iowa City, IA; Mayo Clinic, Rochester, MN.

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33E. Weight loss does not alter sympathetically mediated vascular tone in normotensive obese humans. Alexei V. Agapitov, M.D., Marcelo L. Correia, M.D., *John M. Dopp, Pharm.D.,* Christine A. Sinkey, R.N., Bradley G. Phillips, Pharm.D., William G. Haynes, M.D.; University of Iowa, Iowa City, IA.

PURPOSE: Obesity is associated with sympathoactivation, as assessed by microneurographic muscle sympathetic nerve activity (MSNA). Weight loss has been shown to decrease MSNA. However, it is unclear whether MSNA reflects sympathetic vascular tone.
METHODS: Forearm vascular resistance (FVR) responses to intrabrachial phentolamine (120 µg/min; sufficient to block vasoconstriction to norepinephrine) were used to evaluate the sympathetic contribution to basal vascular tone in 19 obese normotensive subjects (4 males; 39 ± 2 years) and 14 age and gender-matched lean subjects (3 males; 39 ± 2 years). Nitroprusside (10 µg/minute) was used to evaluate vascular smooth muscle dilator responsiveness. Measurements were repeated in all obese subjects after 12 weeks of hypocaloric diet and orlistat treatment and in 8 lean subjects after 12 weeks of observation with no treatment.
RESULTS: Baseline MSNA was significantly higher in obese than lean subjects, but phentolamine responses were similar. The hypocaloric diet significantly reduced body mass index (BMI), blood pressure and MSNA (table; *p<0.05 vs. obese baseline). However, no significant effects of weight loss on vasodilatation to phentolamine and nitroprusside were observed. No significant changes were observed in lean subjects after 12 weeks.

	BMI (kg/m^2)	Daytime mean ambulatory blood pressure (mmHg)	Baselin FVR	Nitroprusside (% Δ FVR)	Phentolamine (% Δ FVR)	MSNA (bursts per minute)
Lean controls baseline	22 ± 1*	91 ± 2	3.3 ± 0.2	-80 ± 2	-58 ± 4	22 ± 1*
Obese baseline	35 ± 1	92 ± 1	2.7 ± 0.2	-75 ± 2	-58 ± 2	30 ± 4
Obese after weight loss	32 ± 1*	89 ± 1*	2.6 ± 0.2	-72 ± 2	-57 ± 3	24 ± 3*

CONCLUSIONS: Elevated MSNA in normotensive obese subjects, and decreases in MSNA with weight loss, do not translate into alterations in sympathetically mediated vascular tone.
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34. Evaluating two approaches for dyslipidemia management: pharmacist-managed lipid clinic and physician-treated patients. *Janet L. Ritter, Pharm.D.*, Canh-Nhut M Nguyen, Pharm.D.; Midwestern University, Downers Grove, IL.

PURPOSE: The purpose of this study is to assess the effectiveness of a pharmacist-managed Lipid Clinic (LC) and primary care physician (PCP) managed patients in attaining the NCEP – ATP III guidelines.
METHODS: The study was conducted in a private outpatient clinic in a group medical practice. All LC patients (age 18 or older) managed by the clinical pharmacist and a stratified random sample of physician treated patients, were enrolled in this retrospective chart-review study. The sample frame included patients who attended one or more office visits with either the LC or their PCP (internist or family practitioner) between June 1, 2001 and December 31, 2001.
RESULTS: One hundred fifty-two LC and 45 PCP patients were enrolled in this study. LDL reduction from baseline for primary prevention, secondary prevention, and diabetes mellitus (DM) resulted in a 28.8%, 30.3%, and 20.6% decrease for LC patients, and a 17.8%, 21.7%, and 11.8% decrease for PCP patients, respectively. LDL and non-HDL goals were achieved in 69% and 59% for LC patients; PCP patients achieved 44% and 44%, respectively.
CONCLUSION: The pharmacist-managed LC is highly effective in achieving the ATP III guidelines; a high percentage of LC patients have attained LDL and non-HDL goals. This may benefit the patient in terms of decreasing their risk for cardiovascular morbidity and mortality. The PCP managed patients compare favorably to national averages in attainment of LDL goals. The presence of the LC may account for the improvement in dyslipidemia management at our medical center.

35. Blood pressure control and factors predicting control in a treatment-compliant veteran population. *Marcel D. Bizien, Pharm.D.*, Sandra G. Jue, Pharm.D., Barry Cusack, M.D., Teri Peterson, M.S.; VAMC, Boise, ID; University of Wyoming, Laramie, WY; Idaho State University, Pocatello, ID.

PURPOSE: To estimate blood pressure (BP) control and identify treatment parameters predicting control in a treatment-compliant, hypertensive, outpatient veteran population.
METHODS: Retrospective review of computerized patient records between April 1, 2000 and October 1, 2001, for demographics, comorbidities, patient-specific BP goals, BP history, current antihypertensive therapy, and refill history. Treatment intensity was calculated based on the dose of each antihypertensive and the number of antihypertensives received. Treatment factors known to influence BP were analyzed via logistic regression.
RESULTS: A total of 250 patients met inclusion criteria. The proportion of patients with a BP < 160/90 was 86%; only 34.8% had a BP < 140/90. Blood pressure control was less common with advancing age (41%, 35% and 28% for patients < 60, 60 to 75, and > 75, respectively; $p<0.01$ for trend). Treatment intensity was highest in those aged 60 to 75, in those with a history of CHF or MI, and lowest in patients > 75 or with a history of stroke. Blood pressure control positively correlated with the number of antihypertensives received (p=0.004 for trend) and long-term simvastatin therapy (p=0.0001). The relationship between simvastatin therapy and BP control persisted after controlling for known confounders. Factors predicting poor control included a BMI > 30 (p=0.018) and advanced age (p=0.0001).
CONCLUSION: In a compliant veteran population, control of BP is poor but more likely in those receiving at least 3 antihypertensives in combination with simvastatin therapy.

36E. Evaluation of angiotensin-converting enzyme inhibitor use in type 2 diabetic patients. *Erin M. Timpe, Pharm.D.*, Naseem Amarshi, Pharm.D., Pamala J. Reed, Dr.P.H., MPH; University of Tennessee, Memphis, TN.

Presented at the Southeastern Residency Conference, Athens, GA, April 26, 2002.

37. Use of billing records to evaluate length of stay, total charges and total costs of patients with chronic heart failure given nesiritide versus standard therapy in a community hospital. *Devon Lewis, Pharm.D., BCPS*, Vikas Gupta, Pharm.D., BCPS; Our Lady of the Lakes Medical Center, Baton Rouge, LA; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX.

PURPOSE: Nesiritide has shown efficacy in management of patients in acute chronic heart failure (CHF), however there is little data on economic impact of patients given nesiritide (N) verses standard therapy (ST) in community hospitals. We evaluated if N compared to ST for CHF patients hospitalized to a monitored unit would result in lower total charges, total costs or length of stay (LOS).
METHODS: This is a non-randomized evaluation. Billing records for 75 patients given N were obtained for: all diagnosis codes, total charges, total costs, financial class, and LOS. Same billing data was obtained for 84 patients in ST group identified from the CHF diagnosis codes of patients given N, and that were in a monitored unit prior to addition of N to the formulary. Total charges and total costs were adjusted for relative weight (RW) of the coded DRG. Outliers were removed based on LOS and the data is presented as mean ± SDEV with $p\leq0.05$ as statistically significant.
RESULTS: Mean RW was similar, 1.50 ± 1.06 for N and 1.50 ± 1.40 for ST, p=0.95. 73% of N patients and 63% of ST patients ST were Medicare/ Medicaid. Mean LOS was higher for N vs. ST, 9.0 ± 7.3 and 6.9 ± 4.3, respectively, p=0.03. Mean RW adjusted total cost was higher for N vs. ST, $7,622 ± $5,301 and $6,875 ± $5030, respectively, p=0.36. Mean RW adjusted total charges were higher for N vs. ST, $15,568 ± $10,791 and $12,987 ± $10,449, respectively, p=0.13.
CONCLUSIONS: This billing analysis found N vs. ST to be associated with a higher LOS and non-significant higher total charges and total costs. Larger controlled studies need to be done to confirm these findings.

38. Bleeding risk in patients on low-molecular weight heparin for anticoagulation in atrial fibrillation. *Sonya Scheuering, Pharm.D., BSNSP*, Minou Khazan, Pharm.D., Ph.D., A. Scott Mathis, Pharm.D.; Saint Barnabas Medical Center, Livingston, NJ.

PURPOSE: To determine the relationship of renal function and low-molecular weight heparin (LMWH) dosing to bleeding and thrombosis in a group of patients anticoagulated for atrial fibrillation (AF).
METHODS: A total of 230 patients receiving LMWH for AF during a 6 month period were retrospectively reviewed and evaluated based on estimated creatinine clearance (CrCl) and dosing (units/kg/day). Renal dysfunction was additionally defined as a calculated estimate of creatinine clearance of ≤ 30 ml/min, or a serum creatinine (SCr) > 2 mg/dL. Thrombosis and bleeding were characterized according to standard definitions.
RESULTS: Any bleeding occurred in 25.3% of patients with renal dysfunction (n=69) and 12.3% of patients with adequate renal function, and dosing was 133.8 ± 53.3 and 137.4 ± 59 units/kg/d, respectively. However, mean CrCl was 41 ± 23.5 and 44.5 ± 24.2 mL/min (p=NS) in patients with bleeding (n=38) and those without, and dosing was 136.4 ± 53.7and 136.3 ± 58 units/kg/day (p=NS), respectively. CrCl and dosing were also similar in patients with and without major bleeding (n=16), but when analysis was restricted to patients with renal dysfunction, the mean dose was actually less in patients with major bleeding (96.5 ± 13.1 vs. 137.3 ± 54.4 units/kg/d; $p<0.001$). In all patients, dosing, but not CrCl predicted thrombosis (n=17). The mean dose in patients with thrombosis was 109.5 ± 40.8 vs. 138.4 ± 57.9 in the other patients (p=0.013).
CONCLUSIONS: Renal dysfunction is a risk factor for bleeding independent of LMWH dose, and lower doses may not protect against thrombosis.

39. Pharmacokinetic interaction study of digoxin and hawthorn. *Roberta Tankanow, M.S.*, Helen R. Tamer, Pharm.D., Daniel S. Streetman, Pharm.D., Scott G. Smith, Janice L. Welton, Thomas Annesley, Ph.D., Keith D. Aaronson, M.D., Barry E. Bleske, Pharm.D., FCCP; University of Michigan, Ann Arbor, MI.

Hawthorn is currently being evaluated for the treatment of heart failure. Beneficial effects may be due to the flavonoid components of hawthorn. However, these components may also affect p-glycoprotein function and cause interactions with drugs that are p-glycoprotein substrates such as digoxin.
PURPOSE: To determine the effect of hawthorn on digoxin pharmacokinetic parameters.
METHODS: Randomized, crossover trial in 8 healthy volunteers evaluating digoxin 0.25 mg alone (D) and digoxin 0.25 mg with hawthorn 450 mg twice daily (D + H) for three weeks. Seventy-two hour pharmacokinetic studies were performed for both treatment groups.
RESULTS: Summary of the pharmacokinetic parameters are shown below (mean ± standard deviation).

Variable	D	D+H	%Change
$AUC_{0\text{-}24}$ (μg•hr/L)	23 ± 4	22 ± 4	-6%
$AUC_{0\text{-}\infty}$ (μg•hr/L)	83 ± 28	73 ± 20	-11%
C_{max} (μg/L)	2.1 ± 0.6	1.8 ± 0.2	-16%
C_{min} (μg/L)	0.84 ± 0.2	0.65 ± 0.2	-22%
C_{max}-C_{min} (μg/L)	1.4 ± 0.7	1.1 ± 0.1	-17%
T_{max} (hours)	1.4 ± 0.4	1.5 ± 0.5	+9%
$T_{1/2}$ (hours)	58 ± 29	50 ± 10	-14%
Cl_{renal} (mL/min)	74 ± 10	81 ± 22	+10%

Overall, serum digoxin concentrations were slightly lower in the D+H group. However, no statistical differences were observed between the two treatment groups ($p>0.05$).

CONCLUSIONS: Hawthorn did not significantly alter the pharmacokinetic parameters for digoxin following three weeks of concomitant therapy. These results also suggest that hawthorn does not significantly alter p-glycoprotein function.

40. Purple grape juice inferior to aspirin as antiplatelet agents. *James J. Nawarskas, Pharm.D.*, Joe R. Anderson, Pharm.D., Joanna Kriehn, M.S., Veena Raizada, M.D.; University of New Mexico, Albuquerque, NM; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: Previous research has shown purple grape juice (PGJ) to have a demonstrable effect on inhibiting platelet aggregation, leading some to question whether or not PGJ may be given in lieu of aspirin, the gold standard antiplatelet agent. However, a direct comparison of PGJ to aspirin has not yet been performed. This study assessed the hypothesis that the antiplatelet effects of PGJ and aspirin are similar.
METHODS: We studied 13 healthy volunteers (mean ± SD age = 25.5 ± 5.9 years) in a randomized, prospective, crossover study. Each subject received 4 treatments (separately) for 4 weeks: PGJ 10 mL/kg/day, PGJ 5 mL/kg/day, white grape juice (WGJ) 10 mL/kg/day, and aspirin 325 mg/day. There was a 4-week washout period in-between treatments. Platelet aggregation was measured at the beginning and end of each treatment period using whole blood impedance aggregometry with collagen (1.0 µg/mL) and arachidonic acid (0.5 mM) as pro-aggregates.
RESULTS: Platelet aggregation in response to collagen was inhibited an average ± SD of 71 ± 22% with aspirin, -5 ± 24% with PGJ 10 mL/kg/day, -11 ± 16% with PGJ 5 mL/kg/day, and –4 ± 18% with WGJ ($p<0.0001$ for all versus aspirin). Arachidonic acid-induced platelet aggregation was inhibited 100 ± 0% with aspirin, 0 ± 33% with PGJ 10 mL/kg/day, 0 ± 13% with PGJ 5 mL/kg/day, and –15 ± 31% with WGJ ($p<0.0001$ for all versus aspirin).
CONCLUSIONS: The antiplatelet effects of PGJ are inferior to those of aspirin. This study also contradicts previous research demonstrating an antiplatelet effect with PGJ. Patients and clinicians should therefore not think of aspirin and PGJ as interchangeable inhibitors of platelet aggregation.

41E. Congestive heart failure therapies within managed care. James Jackson, Pharm.D., Eileen Farrelly, M.P.H., David Ziska, Pharm.D., Feride Frech, R.Ph., M.P.H., *Samantha Hibler*; Applied Health Outcomes; Novartis Pharmaceuticals Corporation, Tampa, FL.

Presented at the 6th Annual Scientific Meeting of the Heart Failure Society of America, Boca Raton, FL, September 23, 2002.

42. Polyamine as the mediator of TNF-α-induced cultured vascular endothelial cell injury. *Shewan M. Aziz, R.Ph., Ph.D., BCOP,* Michal Toborek, M.D., Bennett Yu, M.D., Jay Schwab, R.Ph., BCNSP, James A. Raczek, M.D.; Eastern Maine Medical Center, Bangor, ME; University of Kentucky, Lexington, KY; Henry Ford Hospital, Detroit, MI; Tulane Medical Center, New Orleans, LA.

PURPOSE: Endothelial cell injury/dysfunction is believed to be one of the first events in the development of atherosclerosis. Although ample evidence demonstrates the role of tumor necrosis factor-α (TNF-α) in this process, the specific intracellular signaling mechanism, which mediates cellular injury, has yet to be explored. This study was conducted to determine whether polyamines which play an essential role in cell growth, inflammation, and gene expression, also comprise an obligatory link between the initiating stimuli, TNF-α and changes in endothelial cells responses and metabolism.
METHODS: Cellular polyamine levels as well as polyamine biosynthesis and uptake were measured in cultured porcine pulmonary artery endothelial cells exposed to increasing levels of TNF-α (250, 500 or 1000 U/mL) for 24 hours. In addition, since oxidative stress is involved in a number of TNF-α-mediated effects, cellular oxidation, measured as 2,7-dichlorofluorescein (DCF) fluorescence, and polyamine metabolism were measured in cells treated with TNF-α and/or dimethylthiourea (DMTU), a scavenger of reactive oxygen species.
RESULTS: TNF-α treatment produced a significant increase in the cellular levels of putrescine and spermidine but had no effect on spermine content. An increase in intracellular levels of putrescine and spermidine was correlated with their enhanced uptake into cultured endothelial cells exposed to TNF-α. Treatment with TNF-α also increased endothelial cell activity and mRNA steady state levels of ornithine decarboxylase (ODC), a regulatory enzyme in polyamine biosynthesis. Although DMTU increased ODC activity and mRNA level, it attenuated both TNF-α-mediated oxidative stress and TNF-α-induced disturbances in polyamine metabolism.
CONCLUSION: This data indicates that polyamines may mediate TNF-α-induced cellular responses and that both upregulation of polyamine biosynthesis and transport are involved in this process. In addition, it appears that TNF-α-mediated oxidative stress may be responsible for disturbances in cellular polyamine metabolism.

43. Bioavailability of once-daily dosing of graded-release diltiazem in the morning versus evening. *Sury Sista, Ph.D.*, John C.K. Lai, M.Sc., Okpo Eradiri, Ph.D., Kenneth S. Albert, Ph.D.; Biovail Technologies Ltd., Chantilly, VA.

PURPOSE: The chronopharmacokinetics of a graded release, once-daily diltiazem HCl formulation (GRD) were evaluated to identify variations in morning (7AM or 8AM) vs. evening (10PM) dosing.
METHODS: Single-dose and multiple-dose (once-daily for 7 days), open-label, randomized, two-way crossover studies of GRD 360 mg were completed in 48 healthy, fasting volunteers. Meals and beverages were standardized, and subjects remained seated upright 3 to 4 hours post dose. Serial plasma samples were collected via direct venipuncture up to 48 hours post dose and analyzed for diltiazem and its two major metabolites by HPLC. The primary parameters used to assess the data were $AUC_{0-\infty}$, AUC_{0-24}, AUC 6 AM-12 Noon, C_{max}, and T_{max}. Statistical comparisons using ANOVA were evaluated after logarithmic transformation of dose-dependent parameters.
RESULTS: In the single-dose study, GRD administered in the evening exhibited 17% greater bioavailability compared to morning administration ($AUC_{0-\infty}$ =2830.36 (1114.81 ng/mL vs. 2421.08 [1000.29; p=0.0108]). Mean diltiazem steady-state concentrations were 15% higher following the seven-day administration of GRD 360 mg in the evening compared to administration in the morning (Cave=177.13 [50.79 ng/mL] vs. Cave=153.77 [60.39 ng/mL; p=0.0565]). The evening schedule also provided more than two-fold higher plasma diltiazem levels in the critical morning hours, when both blood pressure and the incidence of cardiovascular events is the highest (AUC 6 AM-12 Noon=1369.67) (430.65 PM vs. 607.30 [260.69ng•hour/mL AM dosing; $p<0.0001$]).
CONCLUSIONS: Administration of GRD in the evening results in greater bioavailability and substantially higher plasma levels of diltiazem between 6 AM and 12 Noon, when blood pressure is highest in most individuals.

44. Pharmacokinetics of eplerenone coadministered with other medications. Dwain S. Tolbert, Ph.D., *Susan E. Reid, M.Ed.*, Barbara Roniker, M.D.; Takeda Pharmaceuticals, Lincolnshire, IL; Pharmacia Corporation, Skokie, IL.

PURPOSE: Hypertensive patients often have additional medical conditions requiring pharmacological intervention. These studies evaluated the pharmacokinetics and safety of the coadministration of eplerenone, the selective aldosterone blocker, with various drug classes.
METHODS: Randomized, placebo-controlled studies in 275 healthy adults and 16 diabetic patients given multiple doses of eplerenone (100 mg QD) coadministered with standard doses of a concomitant medication. Coadministered drugs: cytochrome P450 3A4 (CYP 3A4) substrates (cyclosporine, simvastatin, warfarin, midazolam, Ortho-Novum 1/35®, cisapride, saquinavir); inducers (St. John's Wort); inhibitors (ketoconazole, fluconazole, verapamil, erythromycin); highly protein-bound drugs (glyburide, warfarin); or high renally cleared drugs (digoxin).
RESULTS: Coadministered CYP 3A4 inhibitors increased eplerenone exposure (AUC_{0-24} and C_{max}; $p< 0.05$), clinically significantly (ketoconazole), or statistically significantly (fluconazole, saquinavir, verapamil, erythromycin). Clinically insignificant decreases in eplerenone plasma concentrations were observed with coadministration of CYP 3A4 substrates and inducers. No clinically significant changes were observed when eplerenone was coadministered with highly protein-bound drugs or high renally cleared drugs. Coadministration of all compounds with eplerenone was well tolerated.
CONCLUSIONS: When eplerenone is coadministered with CYP 3A4 inhibitors, eplerenone should be given at the lowest recommended dose (50 mg), except when coadministered with ketoconazole, when the eplerenone dose should not exceed 25 mg. Eplerenone coadministration with CYP 3A4 substrates, inducers, highly protein-bound drugs, or highly renally cleared drugs does not clinically significantly alter the pharmacokinetics of eplerenone or the concomitant medication and does not require dosage adjustment.

45. Safety, tolerability, and pharmacokinetics of eplerenone, a selective aldosterone blocker. Dwain S. Tolbert, Ph.D., *Susan E. Reid, M.Ed.*, Barbara Roniker, M.D.; Takeda Pharmaceuticals, Lincolnshire, IL; Pharmacia Corporation, Skokie, IL.

PURPOSE: The selective aldosterone blocker (SAB) eplerenone reduces blood pressure in patients with mild to moderate hypertension. These studies evaluated the pharmacokinetics, safety, and tolerability of eplerenone in healthy subjects.
METHODS: Data from 7 separate trials (N=181) were used to evaluate eplerenone's pharmacokinetics following single and multiple doses in non-Japanese (n=97) and Japanese subjects (n=60); absorption, distribution, metabolism, and elimination of eplerenone were determined following a single 100 mg oral dose, [^{14}C]-eplerenone (n=8). The effects of high fat food, antacid, and grapefruit juice on eplerenone's pharmacokinetics were evaluated following single 100 mg oral doses (n=16).
RESULTS: Mean eplerenone AUC and C_{max} values increased with increasing eplerenone doses, but the observed increases in plasma concentrations were less than dose-proportional. No statistically significant differences in AUC (90% CI 0.79-1.32), C_{max} (90% CI 0.78-1.05), CL/F, T_{max}, or $T_{1/2}$ were found between Japanese and non-Japanese subjects following single and multiple doses of eplerenone. There was rapid oral absorption of radioactivity following eplerenone. Eplerenone was extensively metabolized with <10% of

the drug eliminated as unchanged eplerenone. Coadministration of a high fat meal, antacid or grapefruit juice did not have a significant effect on eplerenone's rate or extent of absorption.
CONCLUSIONS: This analysis establishes the pharmacokinetic properties of eplerenone and demonstrates that there are no pharmacokinetic differences between Japanese and non-Japanese subjects following single and multiple oral doses of eplerenone. Eplerenone's pharmacokinetics were not influenced by the presence of a high fat meal, antacid, or grapefruit juice. Eplerenone was well tolerated across all groups.

46. Pharmacokinetics of eplerenone in special populations. Dwain S. Tolbert, Ph.D., *Susan E. Reid, M.Ed.*, Barbara Roniker, M.D.; Takeda Pharmaceuticals, Lincolnshire, IL; Pharmacia Corporation, Skokie, IL.

PURPOSE: The selective aldosterone blocker (SAB) eplerenone reduces blood pressure in patients with mild to moderate hypertension. The effects of age, gender, race, and renal or hepatic impairment on eplerenone's pharmacokinetic parameters were evaluated.
METHODS: These studies involved 218 pediatric and adult subjects. Eplerenone dose ranges: 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) and adults with renal impairment. Eplerenone 400 mg QD was administered to adults with hepatic impairment. Single and multiple dose pharmacokinetics were assessed.
RESULTS: There were no statistically or clinically significant differences in $AUC_{0\text{-}24}$, C_{max}, or T_{max} between adult and pediatric patients. No significant differences were observed in eplerenone pharmacokinetics for either race or gender. Statistically significant, but clinically insignificant differences in $AUC_{0\text{-}24}$ were found between adult patients with hepatic impairment and healthy adults (95% CI 1.121, 1.789), or between healthy young and elderly subjects (95% CI 1.2141, 1.7412), or between dialysis patients and healthy adult subjects (95% CI 0.593, 0.921). No significant differences in the incidence of adverse events or clinical laboratory parameters were found between treatment groups.
CONCLUSIONS: Patients with moderate hepatic impairment and subjects older than 65 years had increased eplerenone exposure as reflected in AUC. These increases were clinically insignificant and do not warrant eplerenone dosage adjustments. Renal impairment had no significant effect on eplerenone pharmacokinetics. No statistically or clinically significant differences were observed between pediatric and adult patients. Race and gender had no effect on eplerenone's pharmacokinetics.

47E. The influence of gender and race on pharmacodynamic response to dobutamine during dobutamine stress echocardiography. *Christina L. Aquilante, Pharm.D.*, Larisa M. Humma, Pharm.D., Tara E. Andrisin, B.S., Beatrice Lejeune, B.S., Jannet F. Lewis, M.D., Julie A. Johnson, Pharm.D.; University of Florida, Gainesville, FL; University of Illinois at Chicago, Chicago, IL.

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48. Evaluation of cholesterol goal attainments in patients enrolled in a pharmacist-managed dyslipidemia clinic within a Veterans Affairs medical center. *Melinda E. Micklewright, D.Ph., BCPS*, Roderick D. Teat, Pharm.D.; James H. Quillen Veterans Affairs Medical Center, Johnson City, TN; Pfizer, Inc., Concord, NC.

PURPOSE: To compare the percentage of patients achieving low-density lipoprotein cholesterol (LDL-C) goals in a pharmacist managed dyslipidemia clinic within a veterans administration medical center to the results of LDL-C goal attainment reported in the Lipid Treatment Assessment Project (L-TAP). L-TAP is a multi-center study across the United Stated investigating LDL-C goal attainment.
METHODS: Lipid panel results were reviewed and analyzed for 867 patients receiving dyslipidemia therapy counseling by a pharmacist during a three-month period between January, 2002 and March 2002 . Analysis included utilization of Microsoft Access® for descriptive statistics.
RESULTS: The months of January, February, and March 2002 were independently assessed, in addition to, a composite of all three months. The highest risk category with an LDL-C goal of <100 mg/dl constitute the largest percentage of patients seen with 70.8% of the visits, followed by 26.1% with a goal of <130 mg/dl and 2.9% with a goal of <160 mg/dl. Patients with LDL-C goals <100 mg/dl, <130 mg/dl, and <160 mg/dl achieved their goal 60.1%, 59.8% and 80.0% of the time, respectively. L-TAP reported LDL-C goal achievements of 18%, 37%, and 68% for LDL-C target goals of <100 mg/dl, <130 mg/dl, <160 mg/dl, respectively.
CONCLUSION: Pharmacist managed dyslipidemia clinics could achieve greater LDL-C goal attainment when compared to national prevalence data. Patients in the highest risk category seems to receive the greatest benefit. The results of this research may serve as a basis for the establishment of more dyslipidemia clinics within the veterans administration medical center networks.

49E. Effect of spironolactone in ambulatory heart failure patients receiving conventional therapy. *Alisha D. Vassar, Pharm.D.*, Sharon Starling, R.Ph., Amy Creighton, M.S.; Mercy Medical Center, Springfield, OH; Riverside Methodist Hospital, Columbus, OH; Grant Medical Center, Columbus, OH.

Presented at the Great Lakes Pharmacy Resident Conference, Indianapolis, IN, April 2002.

50E. Aspirin use for primary cardiovascular risk reduction in postmenopausal women. *Devra K. Dang, Pharm.D.*, Gyorgy Csako, M.D., Amy Heck, Pharm.D., Robert Wesley, Ph.D., MacDonald Horne, M.D., Richard O. Cannon, M.D., Robert Lederman, M.D., Frank Pucino, Pharm.D.; Warren G. Magnuson Clinical Center, Bethesda, MD; National Institutes of Health, Bethesda, MD; National Heart, Lung, and Blood Institute, Bethesda, MD; Purdue University, West Lafayette, IN.

Presented at the Eastern States Residency Conference, Baltimore, MD, April 25-27, 2002.

51E. Modulation of potassium currents in a canine model of atrial fibrillation: impact of antioxidant therapy. *Cynthia A. Carnes, Pharm.D., Ph.D.*, Spencer J. Dech, M.A., Tomohiro Nakayama, Ph.D., D.V.M., Jennifer Wierschin, John A. Bauer, Ph.D., Robert L. Hamlin, Ph.D., D.V.M., David R. Van Wagoner, Ph.D.; Ohio State University, Columbus, OH; Cleveland Clinic Foundation, Cleveland, OH.

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52. Patient assessment and modification of risk factors for ventricular arrhythmias prior to the administration of ibutilide. *Anne P. Spencer, Pharm.D.*, Kenneth W. Kenyon, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate the assessment and modification of patient-specific characteristics which portend the development of ventricular arrhythmias with ibutilide administration.
METHODS: A retrospective review of medical records was performed on all patients (n=64) receiving ibutilide at our institution from 1996 to present. Data were collected regarding baseline serum levels of potassium (K^+) and magnesium (Mg^+), pre-conversion QTc interval, and ibutilide dose administered. Assessment criteria included: serum $K^+ < 4.0$ mEq/L without potassium supplementation, serum $Mg^{+2} < 2$ mg/dL without magnesium supplementation, QTc interval > 440 msec, and inappropriate ibutilide dose. Patients were categorized based on the number of risk factors present prior to ibutilide administration. In addition, the prevalence of each risk factor was calculated.
RESULTS: Twenty-seven (42.2%) patients had one risk factor for the development of ventricular arrhythmias present, and 4 (6.2%) had two risk factors present prior to ibutilide infusion. Eighteen (28.1%) patients had a serum $K^+ < 4.0$ mEq/L, however, 5 (7.8%) did not receive supplementation prior to ibutilide administration as indicated. Similarly, 24 (37.5%) had a serum $Mg^+ < 2$, of whom 5 (7.8%) did not receive supplementation. Twenty-six (40.6%) patients had a QTc interval > 440 msec on baseline electrocardiogram. An inappropriate ibutilide dose was utilized in 2 (3.1%) of patients.
CONCLUSIONS: Appropriate patient assessment and risk factor modification occurred in 33 (51.6%) of patients undergoing chemical cardioversion with ibutilide. Information derived from this evaluation will be used to support the development of a process to ensure patient risk-factor modification prior to ibutilide dispensing.

53. Safety and efficacy of ibutilide: experience in a community hospital. *Richard J. Artymowicz, Pharm.D., BCPS*, Suketu Nanavati, M.D., B.J. Cino, Pharm.D., Joseph L. Walker, Pharm.D.; Burdette Tomlin Memorial Hospital, Cape May Court House, NJ.

PURPOSE: This study reviewed the safety and efficacy of ibutilide at a non-teaching, community hospital.
METHODS: Medical records of 52 patients, detailing 56 courses of ibutilide therapy between March of 1999 and May of 2002 were reviewed retrospectively. Patient's past medical history, hospital course, baseline EKG and echocardiographic data, medication use prior to and after ibutilide therapy, conversion rate, and adverse effects were recorded.
RESULTS: Ibutilide led to conversion to sinus rhythm in 46% of patients with atrial fibrillation and 87% of patients with atrial flutter. The average time to conversion was 35 minutes. Nineteen patients experienced an electrocardiographic event within 4 hours of receiving ibutilide, including 2 cases of sustained ventricular tachycardia and 1 case of torsades de pointes. Thirteen of these patients had an identifiable risk factor such as electrolyte imbalance, prolonged baseline QTc, or pretreatment with a Class Ia or III antiarrhythmic. Fifteen patients received ibutilide without adequate washout of a previous antiarrhythmic, with 5 experiencing non-life-threatening arrhythmias within 4 hours of receiving ibutilide. None of the 25 patients who received a class I or III antiarrhythmic within 4 hours of receiving ibutilide experienced a significant electrocardiographic event and 2 reverted back to atrial fibrillation during the admission.
CONCLUSION: Conversion rates and occurrence of adverse events with ibutilide at our community hospital are similar to those reported in the literature. Policy changes to insure electrolyte balance prior to administration of ibutilide and proper weight-based dosing would likely reduce the

occurrence of adverse effects. Early treatment with oral antiarrhythmic agents after ibutilide administration did not result in the development of life threatening arrhythmias.

54. Blood pressure measurement: selection of appropriate cuff size for office and home monitoring. *Deborah S. King, Pharm.D.,* Marion R. Wofford, M.D., M.P.H., T. Kristopher Harrell, Pharm.D., Sara L. Noble, Pharm.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: To identify demographics associated with selection of appropriate cuff size and determine the size most commonly needed for accurate blood pressure (BP) measurement.
METHODS: Consecutive adult patients seen in a hypertension clinic were evaluated over a 2-week period. BP was measured using a mercury sphygmomanometer. Forearm size was determined by measuring midway between the acromial-olecranon process. Cuff size was determined using arm circumference and AHA recommendations: small-adult (<9.5 in), regular-adult (9.5-12.5 in), large-adult (13-16.5 in), thigh (>16.5 in). Data on age, race, sex, and BMI were systematically recorded.
RESULTS: Of the 167 patients assessed, 22% required a regular cuff: all those normal weight (9%, BMI <25) and less than half of those overweight. The majority were overweight (27%, BMI 25–29.9) or obese (65%, BMI >30). A large cuff was required in 48% and 79% of these, respectively, and a thigh cuff in 5% and 11%. No significant differences were found between white males and females in either mean arm circumference (12.5 in) or BMI (28.4). Black females and males had significantly larger arm circumferences (13.5 in; 13 in) and BMI (31.8; 30.7).
CONCLUSIONS: Increased attention should be given to proper cuff size used for office assessment and when recommending equipment for home use. As the incidence of overweight and obesity reach epidemic levels, a regular cuff is not appropriate for the majority of adults. Though equipment is routinely supplied with only a regular cuff, the large cuff is most often needed and should be the standard cuff provided.

55. Differences in the correlations of non-HDL-c and LDL-c with apolipoprotein B in patients receiving pravastatin monotherapy or pravastatin plus cholestyramine. *Eric K. Gupta, Pharm.D.,* Matthew K. Ito, Pharm.D., FCCP, BCPS; University of the Pacific, Stockton, CA; Veterans Affairs San Diego Healthcare System, San Diego, CA.

PURPOSE: Non-HDL-c is a secondary target (NCEP III) in patients with a concomitant elevation in triglycerides and accounts for all the apolipoprotein B-containing lipoprotein particles such as VLDL-remnants, IDL, and LDL. Thus, LDL-c may underestimate apo B concentrations, especially in subjects receiving therapies that may increase triglycerides (i.e. cholestyramine). Therefore, the purpose of this investigation is to compare the difference in correlation between non-HDL-c and LDL-c to apo B in patients receiving pravastatin or pravastatin plus cholestyramine.
METHODS: Fasting lipoprotein profiles from a prior study (Am J Cardiol 1997;80:799-802), involving 59 patients with CHD randomized to either pravastatin monotherapy (20 or 40 mg) or combination pravastatin (10 or 20 mg) plus cholestyramine (8 g) for 12 weeks, was used to determine correlations between apo B with non-HDL-c and LDL-c.
RESULTS: Both non-HDL-c and LDL-c were highly correlated with apo B ($p<0.001$ for all comparisons) in the monotherapy group at baseline (r=0.71, 0.64, respectively) and at 12 weeks (r=0.87, 0.80, respectively), and in the combination therapy group at baseline (r=0.85, 0.84, respectively) and at 12 weeks (r=0.82, 0.69, respectively). Also, non-HDL-c and LDL-c were highly correlated to apo B in patients with triglycerides below the median value of 178 mg/dL (r=0.85, 0.82, respectively), and in patients with triglycerides above the median value (r=0.77, 0.71, respectively).
CONCLUSIONS: Although there were no significant differences between the correlations of non-HDL-c and LDL-c to apo B, non-HDL-c had numerically higher correlations, than LDL-c, with apo B in both treatment groups and across different triglyceride strata.

56. Predictors of warfarin use among Ohio Medicaid patients. J.A. Johnston, *J.C. Cluxton,* P.C. Heaton, J.J. Guo, C.J. Moomaw, M.H. Eckman; University of Cincinnati, Cincinnati, OH.

PURPOSE: Despite demonstrated efficacy in stroke prevention, warfarin is underutilized in patients with atrial fibrillation (AF). We sought to determine the extent and determinants of warfarin use in Ohio Medicaid patients with new-onset AF.
METHODS: We performed a retrospective cohort analysis using Ohio Medicaid administrative billing data that included claims from all institutions, providers, and pharmacies providing services to Ohio Medicaid enrollees. The cohort included all 11,699 continuously enrolled fee-for-service recipients of Ohio Medicaid with a new diagnosis of nonvalvular AF between 1998 and 2000. We determined incipient warfarin use and presence of risk factors for stroke and hemorrhage by searching claims records for corresponding ICD-9-CM and National Drug Codes. Univariate and multivariable analyses were performed to examine the association of risk factors with warfarin use.
RESULTS: Only 9.7% of all patients and 11.9% of those without apparent contraindications filled prescriptions for warfarin in the period from 7 days preceding to 30 days after the development of AF. Hypertension and congestive heart failure independently predicted increased warfarin use. Younger age (<55), older age (≥85), prior intracranial hemorrhage, prior gastrointestinal hemorrhage, predisposition to falls, alcohol/drug abuse, renal impairment, and conditions perceived as barriers to compliance predicted decreased warfarin use.
Multivariable Predictors of Warfarin Use: OR (95% CI)

Age <55 0.73 (0.60-0.90)	Prior GI bleed 0.69 (0.55-0.88)	Prior ICH 0.52 (0.31-0.86)
Age ≥85 0.41 (0.34-0.49)	Hypertension 1.40 (1.23-1.59)	Renal insuff 0.66 (0.52-0.84)
Fall risk 0.61 (0.52-0.73)	Poor compliance 0.84 (0.73-0.97)	
CHF 1.37 (1.20-1.57)	Substance abuse 0.59 (0.35-0.99)	

CONCLUSION: Few in this cohort of Ohio Medicaid patients with incident AF filled prescriptions for warfarin within 30 days of diagnosis. A number of factors, including alcohol or drug abuse/dependence, psychiatric disease, homelessness or inadequate housing, and lack of a caregiver, were both highly prevalent and appeared to bias against warfarin prescription.

57. Use of dobutamine and milrinone in decompensated heart failure patients at a university teaching hospital. *Julie B. Cooper, Pharm.D.,* Debbie Montague M.S., Jo E. Rodgers Pharm.D., J. Herbert Patterson, Pharm.D.; University of North Carolina, Chapel Hill, NC.

PURPOSE: Although, intravenous inotropes are the standard of care for treating decompensated heart failure (HF) patients with low output symptoms, little published information guides inotrope selection. The purpose of this medication use evaluation (MUE) was to determine the potential impact of an inotrope selection algorithm on HF symptoms, duration of therapy, and length of hospitalization at a university teaching hospital.
METHODS: Over a six month period, a prospective MUE was conducted of consecutive patients admitted to a cardiology service who received dobutamine or milrinone for decompensated HF. Data pertaining to agent selection, duration of therapy, and the HF symptom score were collected. An algorithm was constructed based on rational for inotrope selection including risk for hypotension, presence or absence of ischemia, and concomitant medications (β-blockers, hydralazine). Clinical data were compared to the algorithm and analyzed by the Mantel-Haenszel test.
RESULTS: Of the 56 patients assessed (mean age: 61 years, 50% male, mean left ventricular ejection fraction- 26%), 50% of inotrope selection was consistent with the algorithm. While no change in duration of therapy or length of hospitalization occurred, more patients experienced an improvement in HF symptom score after treatment consistent with the algorithm.
Change in Heart Failure Symptom Score after Treatment

	Consistent with algorithm (n=28)	Inconsistent with algorithm (n=28)	p value
Improve	21 (75%)	13 (46%)	0.03
No change	5 (18%)	12 (43%)	
Worse	2 (7%)	3 (11%)	

CONCLUSIONS: An algorithm based approach for inotrope selection in the treatment of decompensated HF may improve patients' symptomatic outcomes.

Critical Care

58. Safety of dexmedetomidine in the clinical setting. *Joseph F. Dasta, M.S.,* Sandra L. Kane, Pharm.D., M.S., Amy J. Durtschi, M.S., Dex Registry Study Group; Ohio State University, Columbus, OH; University of Pittsburgh Medical Center, Pittsburgh, PA; Abbott Laboratories, Abbott Park, IL.

PURPOSE: Since the safety profile of new drugs used in the clinical setting often differs from controlled studies, we compared dosing and adverse drug reactions (ADRs) of dexmedetomidine (Dex) in the naturalistic setting to data from clinical trials.
METHODS: Investigators from eight institutions collected data on 88 patients prescribed Dex as part of sedation therapy.
RESULTS: Only 33% of patients received a loading dose. The initial dosage averaged 0.31 µg/kg/hour (0.1 to 0.7) while the maximum dosage averaged 0.54 µg/kg/hour (0.8 µg/kg/hour in six patients). Duration of therapy averaged 22.1 hours, while 25% received Dex beyond 24 hours. 17% (15 patients) developed hypotension, which is lower than 30% from the package insert. Causality estimates of these patients were: 2 doubtful, 4 possible, 5 probable, and 4 highly probable. Regarding severity, four patients experienced no change in clinical outcome, five required increased monitoring, four required additional laboratory tests, change in vital signs or discontinuing the drug, and three patients required treatment, or experienced an increased length of stay. Bradycardia developed in five (6%) patients, which is similar to 8% from the package insert. Causality estimates of these patients were: 2 probable and 3 highly probable, and all bradycardic patients only required increased monitoring. No patient developed hypertension, while 16% of patients experienced hypertension in clinical trials.
CONCLUSION: Dex was well tolerated and generally administered within

dosing guidelines. The safety profile of Dex used clinically is similar to the package insert. The infrequent use of a loading dose may explain the absence of hypertension.

59. Implementation and evaluation of an intensive insulin therapy protocol in the surgical intensive care unit. *Kelly S. Lewis, Pharm.D.,* David Baldwin, M.D., James A. Colombo, M.D., Lisa Pint, R.N., David M. Rothenberg, M.D.; Rush Presbyterian St. Luke's Medical Center, Chicago, IL.

PURPOSE: The hormonal changes associated with surgical stress induce a number of metabolic changes in both diabetic and non-diabetic patients. Tight glucose control improves outcome in post-surgical patients. There is no standard of care for the management of hyperglycemia. A multidisciplinary team developed and implemented an intensive insulin therapy (IIT) protocol in the SICU. This study documented intraoperative and postoperative compliance with the protocol.
METHODS: A multi-disciplinary SICU team developed a nursing-driven IIT protocol designed to maintain glucose levels between 80 and 120 mg/dL. Surgical house staff and nurses were educated through an inservice program. Protocol compliance was then evaluated prospectively in all cardiac and vascular surgery patients. Appropriateness of IIT initiation and insulin titration were evaluated and episodes of hyperglycemia and hypoglycemia were documented. Reasonable conversions from IV infusion to SQ insulin also were assessed.
RESULTS: 29 patients (9 diabetics) were evaluated over a one month period. Initiation of the protocol in the operating room occurred in 3 of 29 patients, even though intraoperative glucose measurements were > 120 mg/dL in all patients. Appropriate initiation of insulin infusion in the SICU and titration to maintain glucose in the target range occurred in 100% and 83% of patients, respectively. The overall rates of hypoglycemia and hyperglycemic episodes were 2.4 and 19.8 per 100 blood glucose measurements, respectively. IV to SQ insulin conversions were done appropriately in 93% of patients.
CONCLUSION: This study illustrates the effectiveness of a multidisciplinary team approach devised to standardize insulin management in a surgical intensive care unit.

60. Interferon-γ increases dipeptide transport via increased expression of the oligopeptide transporter h-PEPT1 in cultured human intestinal monolayers. *David R. Foster, Pharm.D.,* Christopher P. Landowski, M.S., Lynda S. Welage, Pharm.D., FCCP; University of Michigan, Ann Arbor, MI.

PURPOSE: Intestinal barrier integrity is diminished in critical illness, however alterations in specific routes of permeation are poorly elucidated. The effects of critical illness on the permeation of peptides and peptidomimetric drugs (actively absorbed via the oligopeptide transporter, h-PEPT1) are relatively unknown. We evaluated the impact of interferon-gamma (IFN-γ on h-PEPT1 expression, and peptide permeability in cultured human intestinal monolayers (Caco-2 cells) using the dipeptide glycylsarcosine (Gly-Sar).
METHODS: Caco-2 monolayers were grown on permeable supports at 37ºC. Treated cells were incubated with IFN-γ (50-100 ng/ml) for 48 hours. Total RNA was isolated and RT-PCR was used to determine the expression of h-PEPT1. To assess peptide permeation, treated cells were incubated with IFN-γ (50 ng/ml) for 48 hours. [^{3}H]Gly-Sar (10 µMOL) was added to the apical chambers of the cell supports, basolateral concentrations were serially measured (0-120 min), and effective permeability (P_{eff}) was calculated. Additional experiments were conducted at 4°C to determine the contribution of active transport.
RESULTS: Compared to controls, treatment with IFN-γ 50 and 100 ng/ml increased h-PEPT1 expression by 14.2% and 11.5%, respectively (p=0.019). IFN-γ increased Gly-Sar P_{eff} compared to controls ($7.24x10^{-6} \pm 7.71x10^{-7}$ vs. $5.56x10^{-6} \pm 5.05x10^{-7}$cm/sec, respectively, p=0.034). Inhibition of active transport (4ºC) decreased Gly-Sar P_{eff} by 39.6% in IFN-γ treated cells (p=0.003) and 28.4% in controls (p=0.006).
CONCLUSIONS: IFN-γ increases h-PEPT1 expression in Caco-2 monolayers, resulting in increased permeation of the dipeptide Gly-Sar. These findings imply that intestinal absorption of peptides and peptidomimetric drugs may be increased in some forms of critical illness; this may lead to new strategies to optimize drug/nutrient delivery.

61. Fenoldopam: characterization of use and patient outcomes. *Amy Green, Pharm.D.,* Marc Matthews, M.D., Frank Romanelli, Pharm.D., Tim Clifford, Pharm.D., Kelly Smith, Pharm.D.; University of Kentucky, Lexington, KY.

PURPOSE: Use of the selective dopamine-1 receptor agonist, fenoldopam, has expanded beyond severe hypertension. This may be based on its theoretical improvements in renal perfusion for patients experiencing declining renal function and for prevention of radiocontrast-induced nephropathy. The objective of this study was to characterize the use of fenoldopam at our teaching hospital and describe outcomes related to renal perfusion, including the progression to renal replacement therapy (RRT) after treatment with the agent.
METHODS: A retrospective data analysis of all patients receiving fenoldopam from January 1999 through December 2001 was performed. Investigators systematically documented information regarding patient demographics, indication for use, service prescribing fenoldopam, dose range, and adherence to formulary restriction criteria. Additional data collected included BUN, Scr, urine output, use of diuretics and vasopressors, exposure to nephrotoxic medications, and number of days of RRT.
RESULTS: Of 55 patients reviewed, 9 (16%) received fenoldopam for hypertension, 4 (7%) for prevention of radiocontrast-induced nephrotoxicity (RCN), and 42 (77%) for renal perfusion during declining renal function. No patients in the prevention of RCN group required any form of RRT. Of the 42 patients receiving fenoldopam for renal perfusion, 19% required some form of permanent RRT, 33% necessitated transient RRT, and 48% avoided RRT.
CONCLUSIONS: Specific criteria for initiating therapy and defined endpoints need to be established so that fenoldopam can be used cost-effectively outside of FDA-approved indications. Additional randomized, prospective, human studies are warranted to assess the efficacy of fenoldopam for renal perfusion.

62. Interpreting total, free, and adjusted phenytoin concentrations in medical intensive care patients. *Jeffrey J. Mucksavage, Pharm.D.,* Lingtak-Neander Chan, Pharm.D., John Garofalo, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: This study documented free phenytoin, total phenytoin, and albumin concentrations in medical intensive care (MIC) patients to 1) evaluate the accuracy of the revised Winter-Tozer equation (RWTE) for predicting adjusted total phenytoin concentrations in this population; 2) determine what co-morbid factors may affect the interpretation of these concentrations.
METHODS: Medical records of adults treated with phenytoin or fosphenytoin by the MIC service during the year 2001 were reviewed. Patients were included if free and total phenytoin concentrations were obtained from the same blood sample. Total concentrations were adjusted using the RWTE and compared with the free phenytoin concentration multiplied by a factor of 10, which served as the reference. Demographics, co-morbid conditions, and laboratory values were collected and compared.
RESULTS: Of 28 patients identified, 18 patients were eligible for inclusion. The mean (± SD) adjusted phenytoin concentration determined by the RWTE was 19.6 ± 11.7 mg/L compared to a reference mean of 26.1 ± 15.3 mg/L. The mean predicted error (MPE ± SD) for the equation was -6.52 ± 8.06 and the root mean square error (RMSE ± SD) was 10.19 ± 13.7 (r=0.855). Excluding patients with serum creatinine > 1.5 mg/dL, the MPE and RMSE were -2.91 ± 3.69 and 4.56 ± 5.11, respectively (r=0.983).
CONCLUSIONS: Although well correlated, the RWTE underestimated total phenytoin concentrations when compared to simultaneous free phenytoin concentrations in MIC patients. Worsening renal function is an independent factor that may make this equation less accurate in this patient population.

Drug Delivery

63E. Anticholinergic side effects with long-term transdermal oxybutynin for overactive bladder symptoms. *G. Willy Davila, M.D.,* Roger R. Dmochowski, M.D., Steven W. Sanders, Pharm.D.; Cleveland Clinic Florida, Weston, FL; North Texas Center for Urinary Control, Fort Worth, TX; Watson Laboratories, Inc., Salt Lake City, UT.

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64. Esomeprazole pellets are stable following in vitro suspension in common beverages. *David A. Johnson, M.D.,* Albert Roach, Pharm.D., Anders A.S. Karlsson, Ph.D., Anders S. Carlsson, M.Sc., Dan Behr, Ph.D.; Eastern Virginia Medical School, Norfolk, VA; AstraZeneca, Wayne, PA; AstraZeneca, Molndal, Sweden.

PURPOSE: To determine if esomeprazole pellets from opened capsules are stable when suspended in common beverages.
METHODS: Esomeprazole pellets (0.21 g) were suspended in 100 mL of tap water, milk, orange juice, apple juice or yogurt for 30 minutes in separate USP-certified vessels. To simulate exposure to gastric acid, 500 mL of 0.1 M HCl was added to the suspension. Following a 2-hour incubation, pellets were collected and analyzed using liquid chromatography to determine the percentage of intact esomeprazole pellets.
RESULTS: Esomeprazole pellets were stable after suspension in various beverages and yogurt, but not milk (Table). The low stability of the pellets in milk, which has a high buffering capacity, was due to its near neutral pH that caused dissolution of the enteric-coated polymer of the pellet, release of contents and rapid degradation following acid exposure. Water also has a high pH but no buffering capacity. Thus, when small amounts of the acidic enteric-coated polymer pellets were dissolved in water, the pH decreased rapidly and protected the pellets from further dissolution.
CONCLUSION: Esomeprazole pellets remain stable following in vitro suspension in common beverages. Administration of pellets from an opened esomeprazole capsule in tap water, yogurt, orange juice or apple juice is a practical alternative for patients unable to swallow intact capsules.

Beverage	pH	pH of beverage in 500 mL 0.1M HCl	Stability (Mean % of pellets recovered)
Tap water	7.9	1.2	99
Milk	6.7	1.3	14
Orange juice	3.8	1.3	98
Apple juice	3.2	1.2	98
Yogurt	3.9	1.3	99

65. Physico-chemical stability of L-asparaginase in polyvinylchloride-free bags. *Laurence Guicherd*, Daniel Antier, Pharm.D., Ph.D., Stephanie Dallay, Jacqueline Grassin, Pharm.D.; Trousseau University Hospital, Tours, France.

PURPOSE: Because of the French public purchasing law, drug suppliers often change in hospital. However, the pharmacist has to guaranty the physico-chemical stability of all delivered preparation, especially cytotoxics prepared in centralised unit. Our hospital recently purchased L-asparaginase (ASP) — a cytotoxic agent uses to treat leukaemia — and saline bags polyvinylchloride (PVC)-free used to dilute the drug. Given stability data were lacking, the pharmacy aimed to evaluate the stability of ASP in PVC-free bags.
METHODS: For this study, we used ASP (Labs Aventis, France) and PVC-free saline bags 250 mL (FREEFLEX™, Labs Fresenius, France). Stability parameters were: i) visual control; ii) pH; iii) ASP assay by spectro-photometry (λ=278 nm). All data were compared to bottles of glass (saline, 250 mL). Three concentrations of ASP were tested (13000 UI; 15000 UI; 17000 UI) and preparations were stored at +4°C during the study period and maintained at +20°C for 6 hours before control.
RESULTS: Nor visual aspect perturbation neither significant variation of the concentration (p<0,01) between PVC-free bags and bottle have been observed during the 7-day period of study. We just remarked a pH variation at 24-hour control, followed by a coming back to basal level.
DISCUSSION: Data related to pH measurements suggest an interaction between ASP and both PVC-free bag and bottle of glass, then compensated by the buffer effect of the solution. Nevertheless, ASP appeared to be stable in PVC-free bags over a 7-day period when kept at +4°C and infused at room temperature.

Drug Information

66. A survey of the content of standard response letters. *Joan M. Korth-Bradley, Pharm.D., Ph.D.*, Dominick L. Albano, R.Ph., M.B.A., Carla Perdun Barrett, Pharm.D., Angela E. Bridy-Pappas, Pharm.D., Jacquelyn Collins, Pharm.D., Cassandra Hall-Murray, R.Ph., Arlene C. Santhouse, Pharm.D., Brian Scheckner, Pharm.D., Jill M. Slater, Pharm.D., Mary Tattersfield, R.N., Betsy Woodall, Pharm.D., BCPS, Marcy Yanchunas, Pharm.D.; Wyeth Pharmaceuticals, Philadelphia, PA.

INTRODUCTION: As a tool to delivering high quality and consistent information to the public, the medical communications departments of pharmaceutical companies develop standard response letters (SRLs) that are sent to health care providers who request information. Requests for information must be unsolicited and the SRLs must be complete and provide balanced information.
PURPOSE: The purpose of the study was to evaluate the format and content of SRLs provided in response to pharmacists' questions.
METHODS: A sample of 19 SRLs had been obtained from a variety of pharmaceutical companies, including our own, in a single-blinded method. Questions were posed for information, that could not be not answered by the package insert (PI), by callers who identified themselves as pharmacists in either hospital or community practice. The SRLs were then reviewed by a committee of medical communications staff including those who use SRLs to respond to questions from callers, assessing the question, presence or absence of summary bullets, the format of the body of the SRL, presence or absence of conclusions, presence or absence of disclaimer about the approved indication and references.
RESULTS: Twenty-one (21%) of the SRLs did not directly respond to the question asked. A further 10% used a combination of two or three SRLs to provide a response that was incompletely addressed in either SRL. Summary bullet points were found in only 10% of SRLs. The median length of the SRLs was 3 pages with a range of 1 to 7. Few of the SRLs did more than summarize clinical studies. Only 26% contained a synthesis or summary of the evidence and only 16% of the SRLs had a conclusion in response to the question posed. There was universal use of disclaimers, reminding the reader of the SRLs as to the fact that the information provided may not have been contained in the PI. The PI was always enclosed with the SRL as was additional material in 32% of cases. Enclosures included copies of published papers, abstracts, and literature searches. Unpublished data on file was cited in the reference section in 26% of cases while 10% of the SRLs cited no references at all.
CONCLUSIONS: There is a wide variety in the quality of standard response letters. At best, they are a thorough, balanced review of the literature, including unpublished company-sponsored studies. In other cases, they were simply a listing of articles obtained in a literature search. SRLs may provide access to data not available in the published literature and thus may offer additional information to clinical pharmacists.

67. Evaluation of drug safety-related knowledge, attitude, and behaviors among college students in Taiwan. *Fei-Yuan Hsiao, M.S. candidate*, Yi-Chun Chiang, B.S., Wuan-Jin Leu, B.S., Ying-Chi Lin, 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, attitude, and behaviors towards to drug safety and pharmacist's role in first year college students in Taiwan.
METHODS: A total number of 148 departments in 25 universities were sampled by stratified randomization. Three sections of questionnaire were designed and validated. The first section included 10 dichotomous questions to test the knowledge of drug safety. The attitude and trustiness to pharmacists were also evaluated by 3 questions and 1 question in 5-point scale. The final section contained 10 questions in a 5-point scale to access the behaviors related to safe use of drug.
RESULTS: Out of 6820 forms, 6270 was completed with a completed rate of 91.9%. Mean score of knowledge was 6.55 ± 2.25 for all responders, and 6.47 ± 2.28 and 7.00 ± 2.01 for non-health science and health science related students, respectively ($p<0.05$). The students showed positive attitude and trustiness toward pharmacists' profession with a mean score of 12.64 ± 2.19 and 3.59 ± 0.70. Average behavior score was 34.06 ± 4.09 with a perfect score of 50, indicating warranty of efforts to improve the safe use of medications. However, students major in different health professionals showed distinct levels of trustiness to pharmacist. Mean score were 3.54 ± 0.69, 3.93 ± 0.66 and 3.69 ± 0.62 for medical, pharmacy, and nursing students, ($p<0.001$).
CONCLUSION: College students, as a sample representing well-educated public, are still in a lack of appropriate knowledge, attitude and behavior related to safe use of drug. Pharmacists should take a more active role to provide education for medication safety in Taiwan.

68. Medication use evaluation of fenoldopam at a major teaching institution. *Ann L. Adams, Pharm.D.*, Michelle A. Leady, Pharm.D.; University of Michigan Health-System, Ann Arbor, MI.

BACKGROUND: Fenoldopam mesylate is a dopamine D_1-like receptor agonist that vasodilates the peripheral and renal vasculature resulting in its ability to be successfully used in patients with severe or malignant hypertension. Its renal vasodilatory effects offer an advantage over other agents commonly used for malignant hypertension and have expanded its potential use to include prevention of nephropathy in patients at risk of contrast media-induced renal dysfunction. In February of 1999, fenoldopam mesylate was approved by the pharmacy and therapeutics committee at our institution with restriction to specific criteria due its higher cost compared to alternative agents.
PURPOSE: A medication use evaluation was performed to determine whether adherence to approved restrictions had occurred.
METHODS: All patients that received fenoldopam were included in this retrospective review. Review of information contained in an electronic database was performed.
RESULTS: One hundred forty-one patients received fenoldopam between February 1, 1999 and January 31, 2002. Appropriate use occurred in 130/141 (92.2%) patients. Approval from one of the approving services was not obtained in 11/141 (7.8%) cases. Adverse events reported for fenoldopam included headache, somnolence, nausea, vomiting, abdominal pain and hypotension. The total drug cost for fenoldopam during this time was $364,826.54, which included $15,568.45 for unapproved uses.
CONCLUSION: With few exceptions, adherence to restrictive criteria occurred with fenoldopam, limiting the financial impact to our institution.

Education

69. Are pharmacoeconomic fellowship programs adhering to American College of Clinical Pharmacy guidelines? *Vittorio Maio, Pharm.D.*, Jennifer H. Lofland, Pharm.D., M.P.H.; Thomas Jefferson University, Philadelphia, PA.

PURPOSE: 1) To describe the extent to which pharmacoeconomic (PE) fellowships adhere to American College of Clinical Pharmacy (ACCP) guidelines developed in 1999. 2) To determine whether programs established before and after 1999 differ in compliance with guidelines.
METHODS: A 28-item survey was administered to preceptors via the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Web site. Preceptors were identified via ACCP and ISPOR fellowship directories as well as ISPOR's Web site and membership roster. Preceptors currently involved in a program were included in the analysis. χ^2 and Fisher's exact tests were performed.
RESULTS: Forty-nine preceptors completed the survey and 38 met inclusion criteria. Of these, 82% were involved in a program established prior to 1999. Overall, 97% of preceptors had an advanced degree, 89% had a strong PE experience, and 79% had an established record in the field. Preceptors indicated programs were at least two years in length (84%), with available resources such as a medical library (97%), a computer center (87%), and a clinical research center (66%). Programs provided fellows with research skills

including the conceptualization (82%), administration (71%), and data management (85%) of research projects. However, only 32% of programs devoted 80% or more of the fellow's time toward applied PE research activities. There were no statistically significant differences in adherence to guidelines between programs established before and after 1999.
CONCLUSIONS: PE fellowships appear to adhere to ACCP guidelines, although more programs need to provide additional applied research activities. Continued refinement and evaluation of the guidelines are needed.

70. Utilizing a self-administered health awareness questionnaire to increase clinic educational efforts. *Deborah S. King, Pharm.D.,* Marion R. Wofford, M.D., M.P.H., T. Kristopher Harrell, Pharm.D., Sara L. Noble, Pharm.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: A pilot study was undertaken in a hypertension specialty clinic to evaluate 1) the utility of employing a routine cardiovascular risk factor health awareness survey as an initial educational tool and 2) patient awareness of desired health "numbers."
METHODS: A survey instrument consisting of 5 multiple-choice questions assessing awareness of desired health "numbers" was developed and initially tested outside the clinic. Within the clinic, during a typical 2-week period, randomly selected patients were asked by the receptionist to complete the survey. After entering the examination room, clinic providers were instructed to simply collect the survey while volunteering no discussion or validation of accuracy of the results unless initiated by the patient. A survey instrument was requested and completed on 88 patients.
RESULTS: While awareness of desired health "numbers" was less than ideal, virtually all patients completing the survey initiated discussion and requested additional information, especially regarding personal "numbers." An appropriate blood pressure value was correctly identified by 86%, desirable blood sugar by 55%, and desirable cholesterol values by 51% of patients. Of those with diabetes, 82% correctly identified desirable blood sugar values, while of those with dyslipidemia, only 47% were able to identify desirable cholesterol. Though 92% of the population were overweight or obese, only 21% could identify an appropriate BMI goal.
CONCLUSIONS: Assessing awareness of healthy "numbers" via a self-administered survey offers one possibility for increasing provider and patient recognition of the need for subsequent education efforts. Simple measures, including surveys, can increase patient awareness and health consciousness.

71. Survey of toxicology and emergency medicine training in U.S. schools of pharmacy. Amy Toxcano, B.S., Heather M. Eyrich, Pharm.D., Frank L. Hughes, Pharm.D., *Kevin O. Rynn, Pharm.D.*; Rutgers University, Piscataway, NJ.

PURPOSE: To provide information on education and training in toxicology and emergency medicine (EM) at schools of pharmacy in the United States (US).
METHODS: Eighty-one surveys were mailed to the Schools of Pharmacy in the US in February 2001. Surveys requested information pertaining to toxicology course work and experiential learning in toxicology and EM. Second requests were mailed to capture non-responders.
RESULTS: Sixty-eight out of 81 (84%) surveys were returned. Sixty-six percent offered toxicology in their curriculum. Seventy-nine percent had a stand-alone course while 21% offered toxicology as part of another course. Sixty percent of the toxicology course work was required, 35% was elective, and 5% had both required and elective course work. Ninety percent of programs offered toxicology in the 2nd or 3rd professional year. Total credits averaged 2.4. Up to 11 instructors taught the toxicology courses. Experiential rotations were offered in EM from 37% of responders and in toxicology by 56%. Two (8.7%) EM rotations were required and no toxicology rotations were required. EM preceptors took an average of 4.7 students/year, toxicology preceptors 7.8 students/year. Preceptors instructed between 1-4 students per rotation. Fifty percent of preceptors were adjunct faculty, 22% full-time tenure track, 7% full time clinical track, and 21% responded other.
CONCLUSIONS: Toxicology and EM are curriculum topics that require attention, particularly during the United States' war on terror. Schools of Pharmacy offer education in these areas, however programs should review their curriculum to ensure graduates are prepared for today's practice environment.

72. Impact of a pharmacist-led group anticoagulation education class on patient outcomes. *Carrie L. Johnson, Pharm.D.,* Fran A. Trenaman, Pharm.D.; Group Health Associates; University of Cincinnati, Cincinnati, OH.

PURPOSE: This study's purpose was to measure the benefits that patients may gain from receiving education from a one-time group class taught by a pharmacist regarding warfarin therapy. The study compared the following outcomes: 1) the time patients remained within their goal INR range; 2) the time between PT/INR laboratory blood draws, 3) the number of PT/INR lab draws and adherence to a minimum of monthly monitoring, 4) the frequency of dosage adjustments, and 5) adverse events with warfarin therapy.
METHODS: Medical records of 142 patients on warfarin therapy were evaluated. Patients were reviewed over a twelve month period during 2001 and 2002. 68 patients not attending the class were compared to the 64 study patients that attended the class. The non-warfarin educated patients were randomized using a random order table.
RESULTS: In the latter six months, patients who attended the warfarin education class had statistically significantly smaller time lapses between INR laboratory blood draws ($p=0.02$). Also in the study's second six months, the percentage of INR values within the target range was significantly higher in the group of patients who had attended the class than in the group that did not ($p=0.02$). The patients who attended the class also had fewer adverse events and fewer deviations from the target INR range.
CONCLUSION: The results indicate that a group anticoagulant education class led by a pharmacist increased patient adherence to monthly monitoring, increased the frequency that INRs were within therapeutic range, and decreased large variations from the desired INR ranges.

73. Evaluation of the utilization of game-based teaching strategies in a pharmacotherapeutics course. *Dennis Parker, Jr., Pharm.D.,* Denise Rhoney, Pharm.D.; Wayne State University, Detroit, MI.

PURPOSE: Discussion sessions are traditionally based upon passive learning, although active learning may be more effective as it promotes critical thinking and integration of knowledge. We implemented a game-based learning tool called "Central Nervous System (CNS) Survivor" in the second professional year pharmacotherapeutics course. A student satisfaction survey was given to assess student attitudes towards the game.
METHODS: Students were divided into 4 groups which were named based upon the lobes of the brain. The groups competed against each other in a 4-game series of "challenges", similar to the popular television game, during designated discussion sessions of the CNS module. The challenges emphasized teamwork and an extensive review of the material via a multi-media approach. A student satisfaction survey consisting of 38 items was employed upon completion of the game. Likert Scales (1-4) were used to evaluate the perception and effectiveness of this teaching tool. Descriptive statistics were used to evaluate the responses.
RESULTS: All students in the class (n=113) completed the survey. The majority of students attended all games (83%). Although 86% of students listed extra credit as a reason for attending, most (77%) said they would have attended if extra credit were not awarded. Most students (56%) indicated that reviews in previous classes had not been helpful and almost all (92%) preferred active learning. Over 75% of students thought that the game was useful in improving teamwork, critical thinking skills, and scores on examinations. Overall, 99% were satisfied with the game and 97% felt that "CNS Survivor" was an innovative teaching tool.
CONCLUSIONS: The use of game based discussion sessions can promote active learning and better retention than traditional lecture based reviews. Innovative teaching strategies such as gaming can be used to create an environment of enjoyment which improves student's perception of learning. Validation of active learning via subjective measures deserves further investigation.

74. Development and evaluation medication teaching service for hospitalized cancer patients. Moon H. Shin, M.S., Jung M. Oh, Pharm.D., Kyong J. Jeong, M.S., Seung K. Choi Ph.D.; Pochon CHA University, Kyonggi-do, Korea; Sookmyung Women's University, Seoul, Korea.

PURPOSE: The purpose of this study was to develop and evaluate the optimal patient education guideline for cancer patients receiving chemotherapy in the hospital.
METHODS: Patient medication teachings including verbal instruction and written materials were provided by a pharmacist for cancer patients receiving chemotherapy on the first or second day of hospitalization. After providing medication teaching a written survey was performed in order to measure the patient's satisfaction with the medication teachings and to evaluate the effectiveness of the patient medication teaching.
RESULTS: Verbal patient medication teachings and written materials covering the topics of the cancer, chemotherapy agents and adverse effects were provided for hospitalized cancer patients receiving chemotherapy. This individual patient medication teaching was provided at bedside of hospitalized cancer patients. Written surveys were also performed in all patients after the medication teaching was completed. The results of 37 written surveys revealed that almost all patients (96.3%) felt that medication teaching is a must in order to understand and accept the chemotherapy by cancer patients. In addition, almost all patients (92.6%) stated that they were extremely satisfied with the medication teaching provided by the pharmacist. The levels of understandings on the chemotherapeutic agents ($p<0.05$), side effects of chemotherapeutic agents ($p<0.05$), and symptoms of cancer ($p<0.05$) were significantly higher after the patient medication teaching was provided.
CONCLUSIONS: The results of this study show that a well-developed patient medication teaching by a pharmacist for cancer patients can increase the level of medication knowledge, which would ultimately increase patient's medication compliance rate.

75. Meta-analysis of medication adherence interventions in the pharmacy setting. *Liza Takiya, Pharm.D.,* Andrew M. Peterson, Pharm.D., Rebecca Finley, Pharm.D.; University of the Sciences in Philadelphia; Philadelphia College of Pharmacy, Philadelphia, PA.

PURPOSE: To examine the effect of pharmacy-based interventions targeting medication adherence and identify successful interventions.
METHODS: Literature search was performed between 1970-December, 2000 using Medline, IPA, PsychLit, ERIC, and Embase. Randomized, controlled trials written in the English language with at least 10 subjects per group were screened. Further, the intervention must have been directed toward a patient or caregiver and the article must have reported adequate adherence and sample size data. Each article was reviewed by two reviewers and entered into a database. All adherence measures were converted to common effect size (ES) using Cohen's d or d'. A random effects model was employed and the ANOVA and Q-test were used for statistical testing. Any $p<0.05$ was considered significant.
RESULTS: Seven articles, totaling 1201 patients were identified. Four of the seven articles studied more than one intervention, yielding 14 separate intervention groups. Six interventions were behavioral (BI), two were educational (EI), and six were a combination (CI) of EI and BI. Hypertension was the most common disease state (n=5). Mean intervention duration was two months (< 1 month-6 months). The Q-test supported homogeneity for all groups. The overall ES was 0.8. The ES for each intervention type was 0.05 (95% CI, -0.03-0.12), 0.03 (95% CI, -0.13-0.2), 0.14 (95% CI, 0.04-0.24) for the BI, EI, and CI, respectively.
CONCLUSIONS: The combination of educational and behavioral interventions was most successful in enhancing medication adherence. More well-designed studies need to be performed regarding medication adherence interventions in the pharmacy setting.

76E. The impact of supplemental instruction sessions in a problem-based learning curriculum. *Brandon J. Sucher, Pharm.D.,* Brian Crabtree, Pharm.D., BCPP; Palm Beach Atlantic College, West Palm Beach, FL; University of Mississippi, Jackson, MS.

Presented at the Annual Southeastern Residency Conference, Athens, GA, April 2002.

77. Influence of a pharmacist-managed diabetes self-management education service on patient behavioral outcomes. *L. Brian Cross, Pharm.D., CDE,* Diane Pojanowski, Pharm.D., Jennifer Campbell, Pharm.D., CDE, Gale Hamann, Pharm.D., BCPS, CDE; University of Tennessee Health Science Center; Regional Medical Center, Memphis, TN.

PURPOSE: The purpose of this research was to evaluate the influence of a pharmacist-managed diabetes self-management education (DSME) Service on behavioral outcomes in patients with diabetes.
METHODS: A retrospective study was done to evaluate 163 patients who attended a pharmacist-managed DSME during the year 2001. Patients were contacted by telephone within 6 months of completing DSME for follow-up assessment of changes in lifestyle behavioral goals set during DSME. Behavioral goals were assessed by frequency of occurrence: all of the time, most of the time, some of the time, never.
RESULTS: Patient goals for changes in lifestyle behavior were represented by seven categorical topics: glucose monitoring, skipping meals, exercise, carry fast acting glucose for hypoglycemia treatment, dietary changes, examine feet regularly, record glucose and bring log to physician appointments. At least 63% of patients reported meeting behavioral goals set during DSME all of the time or most of the time for all goals except the topic of changes in exercise patterns (bring log to physician appointments 93%, examine feet regularly 91%, change in diet 77%, do not skip meals 72%, carry fast acting glucose source 66%, monitors glucose 63%). Fifty-four percent of patients stated they had made changes in exercise patterns only some of the time or never.
CONCLUSIONS: A pharmacist-managed DSME Service may influence behavioral changes in patients with diabetes through increasing patients' awareness of important self-care issues.

Endocrinology

78E. Clinical outcomes of a pharmacist-managed diabetes self-management education service. Diane Pojanowski, Pharm.D., *L. Brian Cross, Pharm.D., CDE,* Jennifer Campbell, Pharm.D., CDE, Gale Hamann, Pharm.D., BCPS, CDE; University of Tennessee Health Science Center; Regional Medical Center, Memphis, TN.

Presented at the 33rd Annual Southeastern Residency Conference, Athens, GA, April 2002.

79. Relationship of gender and obesity to youth-onset type 2 diabetes. *William D. Linn, Pharm.D.,* Thomas C. Shank, Pharm.D.; University of Texas; Pfizer Pharmaceuticals, San Antonio, TX.

PURPOSE: Studies have shown an increasing prevalence of type 2 diabetes in pediatric patients with diabetes. Most of these patients' body mass index (BMI) exceeded the 85th percentile and there was a higher prevalence in females. This study evaluates this relationship in a predominantly Hispanic population.
METHODS: In December 2001 a diabetes screening project was performed in San Antonio, TX. Data were collected on demographics, vital signs, a full lipid profile, and a random or fasting glucose. A Body Mass Index (BMI) was calculated using the formula: BMI = wt in Kg/Ht in meters^2. Glucose intolerance was defined as having a random glucose > 140 mg/dL or a fasting glucose > 110 mg/dL. The data were imported into a relational database (Access) for analysis.
RESULTS: A complete data set was available for 530 patients < 18 years of age. There were 282 males and 248 females. For those with a BMI < 27, 15% of the males and 18% of the females exhibited glucose intolerance. For the cohort with a BMI $ 27, 14% of the males and 24% of the females had glucose intolerance.
CONCLUSIONS: These data are concordant with other data that there is a gender bias in youth-onset type 2 diabetes. This may relate to differences in endurance activities and their effects on insulin sensitivities. Pharmacists need to be aware of the increasing prevalence of type 2 diabetes in this population and the implications for using oral hypoglycemic medications in adolescents.

80. Evaluation of metformin utilization and subsequent formulary removal in a community hospital setting. *Jacqueline L. Fein, Pharm.D., BCPS,* Marc I. Sandberg, M.D., Tom Ollis, R.Ph., M.S.,CHE; Rutgers University, Piscataway, NJ; Hunterdon Medical Center, Flemington, NJ.

PURPOSE: Despite specific contraindications provided by the manufacturer, studies of prescribing patterns suggest that 25-50% of patients at risk for lactic acidosis are prescribed metformin. We evaluated metformin utilization in our institution because of patient safety concerns. Based on our results, the Pharmacy and Therapeutics Committee removed metformin from the formulary. We present utilization patterns of metformin both before and after its removal from formulary in a community hospital setting.
METHODS: Medical records of patients prescribed metformin over two separate 2-month time periods (before and after formulary removal) were reviewed. Information including patient age, gender, physician, schedule, and adverse drug event occurrence was collected. Each record was reviewed for metformin contraindications and conditions causing hypoxemia, which may increase the risk of lactic acidosis.
RESULTS: The preliminary review contained data for 33 inpatients. Potential risk for lactic acidosis was detected in 27.2% (9/33) of patients. Some identified risk factors included sepsis or pneumonia (9%, 3/33), acute cardiac conditions (6%, 2/33), contrast studies (6%, 2/33), and elevated serum creatinine (3%, 1/33). After metformin formulary removal, potential risk for lactic acidosis was detected in 14.2% of patients (2/14) prescribed metformin. No adverse drug events were noted during the study period.
CONCLUSION: Our initial study demonstrated inappropriate metformin prescribing in 27% of reviewed patients. This trend was reduced after formulary removal of metformin and physician education. We will continue to monitor our patients for inappropriate utilization of metformin and provide education regarding specific contraindications.

81. Evaluation of men's knowledge and perceptions of osteoporosis risk and lifestyle modification. *Sheryl L. Follin, Pharm.D., BCPS,* Laura B. Hansen, Pharm.D., BCPS, Robert L. Page, Pharm.D., BCPS; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: The purpose of this study was to evaluate men's knowledge of risk factors for osteoporosis, beneficial exercises, and calcium/vitamin D intake; their perceived level of risk, and actual risk for osteoporosis.
METHODS: One hundred community dwelling men ≥ 18 years of age were surveyed by a pharmacy healthcare provider for demographic data; personal risk factors; and osteoporosis knowledge regarding risk factors, exercises, and appropriate calcium and vitamin D intake.
RESULTS: Eighty-one percent (age 52 ± 17 years, range 18-86) had knowledge of osteoporosis. Twenty-seven percent perceived they were at risk, but most felt it was low. Thirty-four percent had ≥ 3 osteoporosis risk factors. The majority of subjects correctly identified the following risk factors: low calcium (85%), inactivity (77%), family history (71%), personal fracture history (60%), and smoking (56%). Many did not identify low testosterone (65%), Caucasian race (62%), high caffeine (60%), and excessive alcohol consumption (54%) as risk factors. Sixty-seven percent incorrectly chose obesity as a risk. Most incorrectly identified swimming (80%) and cycling (69%) as bone-building exercises. Seventy percent did not know the recommended consumption of calcium and vitamin D. Fifty-four percent, 16%, and 9% reported taking a daily multivitamin, calcium supplements, and vitamin D supplements, respectively. Patients taking calcium supplements appeared more knowledgeable about osteoporosis risk.
CONCLUSION: Most men understand a working definition of osteoporosis, but knowledge and perceptions of risk factors and lifestyle modifications are lacking. Pharmacists can play an important role in educating men about osteoporosis risks and interventions.

82. Screening and identifying impaired fasting glucose in high-risk patients in the community pharmacy setting. *Brian K. Irons, Pharm.D., BCPS,* Arthur Nelson, Ph.D., Kathleen A. Snella, Pharm.D., BCPS, Rebecca B. Sleeper, Pharm.D., BCPS, Maumi Villareal, M.S.; Texas Tech University Health Sciences Center, Amarillo, TX.

PURPOSE: The ADA recommends screening for impaired fasting glucose (IFG) in patients at an increased risk for the development of type 2 diabetes. The goal of this study was to document the ability of pharmacists in the community setting to identify patients with IFG. The primary objective was to determine the frequency of IFG among high-risk patients identified and screened. A secondary objective was to assess patient characteristics that correlate with a positive IFG screen.
METHODS: Patients at risk for type 2 diabetes, assessed via a predetermined rating scale using known diabetes risk factors, were identified in participating community pharmacies in Texas. Patients at least 18 years of age were included if they scored ≥ 10 on the rating scale, were fasting at least 8 hours, and if fasting plasma levels were < 126 mg/dl. Patients were categorized with having IFG (110-125 mg/dl) or normal glucose (< 110 mg/dl). Univariant analysis was used to determine patient characteristics that correlated with a positive screen for IFG.
RESULTS: A total of 575 patients were screened. Forty-six of 252 (18.2%) patients who met the inclusion criteria were identified as having IFG. No demographic, diabetes risk factor or lipid parameter specifically correlated with a positive IFG screen.
CONCLUSIONS: Screening high-risk patients in the community pharmacy setting may be an effective way to identify patients with IFG as nearly one in five patients in this setting screen positive. Identifying these patients is important secondary to their significant risk of developing diabetes.

83. A retrospective evaluation of performance measurements in adult patients with diabetes mellitus. *Francine A. Farnsworth, Pharm.D.,* Brigitte L. Sicat, Pharm.D., BC-ADM, Patricia M. Selig, M.S., FNP, CDE; Virginia Commonwealth University; Medical College of Virginia, Richmond, VA.

PURPOSE: In April 2001, the American Medical Association, the Joint Commission on Accreditation of Healthcare Organizations, and the National Committee for Quality Assurance developed a consensus statement on coordinated performance measurements for the management of adult patients with diabetes. This study evaluated selected performance measurements to assess and improve the quality of care received by patients at an interdisciplinary Internal Medicine Clinic.
METHODS: A retrospective chart analysis was performed on 288 randomly selected patients who had ≥ two visits with an ICD-9 code for diabetes between September 1, 2000 and August 31, 2001. Patient records were reviewed for the most recent blood pressure, HbA_{1c}, and lipids. Documentation of aspirin, ACE-I, and lipid lowering therapy was also recorded. Candidates for aspirin, ACE-I, or lipid lowering therapy not receiving treatment were evaluated for the documentation of a contraindication to drug use.
RESULTS: The percentage of patients with SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg were 57% and 18%, respectively. Of patients with documented laboratory values, 68% had a HbA_{1c} ≥ 7% and 59% had an LDL ≥ 100 mg/dL. Of patients without contraindications to therapy, 51% of patients had no documentation of aspirin, 29% had no documentation of ACE-I use, and 39% of patients with LDL ≥ 100 mg/dL were not receiving lipid lowering therapy.
CONCLUSIONS: The results of this study revealed that SBP, glycemic control, and LDL were not optimally controlled in over 50% of patients. This study will be used to develop interventions to improve the quality of care received by patients with diabetes at our clinic.

84. Comparison of efficacy between acipimox and fenofibrate in patients with hyperlipidemia. *Jung M. Oh, Pharm.D.,* Seungmi Kim, M.S.; Sookmyung Women's University, Seoul, Korea.

PURPOSE: The objective of this study was to compare the efficacy of acipimox and fenofibrate for the treatment of hyperlipidemia.
METHODS: This study performed a retrospective comparison of acipimox (250 mg PO TID) and fenofibrate (200 mg PO qday) by comparing the means of changes in total cholesterol, triglyceride, HDL-C, LDL-C, and TC/HDL-C ratio at 3, 6, and 9 months of the treatments.
RESULTS: A total of 103 patients (41 in acipimox group and 62 in fenofibrate group) were evaluated. In general, acipimox- and fenofibrate-treated groups were comparable with respect to demographic characteristics. After treatments both acipimox and fenofibrate produced a significant reduction in total cholesterol from baseline (9.7% with acipimox; 11.3% with fenofibrate) and triglyceride levels (52.6% with acipimox, $p<0.001$; 54.3% with fenofibrate, $p<0.001$). HDL-C levels after treatments increased by 8.4% and 9.3% with acipimox and fenofibrate, respectively. The mean changes of total cholesterol, triglyceride, HDL-C were not significantly different between the two treatment drugs. The mean changes of LDL-C levels were 4.4% with acipimox and 2.0% with fenofibrate after treatments. There was a significant reduction in TC/HDL-C ratio from baseline for both drugs (15.2% with acipimox; 18.0% with fenofibrate), and the reduction of TC/HDL-C ratio was not significantly different between the two drugs ($p>0.05$).
CONCLUSIONS: Both acipimox- and fenofibrate- treated groups experienced significant changes in total cholesterol, triglyceride, HDL-C, and TC/HDL-C ratio from the baseline after treatments. However, LDL-C levels did not change significantly in both groups. The changes in total cholesterol, triglyceride, HDL-C, LDL-C and TC/HDL-C ratio between acipimox and fenofibrate treated groups were similar.

85. Rapid weight gain with thiazolidinediones: results from a meta-analysis. *Elaine Chiquette, Pharm.D.,* Michael Dolker, Ph.D., Charles Lucas, M.D.; Aventis Pharmaceuticals, Bridgewater, NJ; Roche Laboratories, Nutley, NJ.

PURPOSE: TZDs activate PPAR-γ causing pre-adipocytes to differentiate into mature fat cells. We conducted a meta-analysis to quantify the weight gain observed within 6 months of initiating TZDs as monotherapy or combination therapy.
METHODS: English citations were identified through December 2001 from 3 electronic databases, references of pertinent articles, ADA abstracts and manufacturers. We limited our review to randomized controlled trials (RCTs) that lasted at least 12 weeks and compared TZDs monotherapy or in combination to placebo. We adopted the DerSimonian and Laird empirical Bayes random-effects estimator to calculate the pooled measures of TZDs effect on weight.
RESULTS: Only 11 RCTs reported the impact of TZDs on weight (6 rosiglitazone and 5 pioglitazone). The heterogeneity testing identified 4 trials as significant outliers. Most of these trials (3/4) were conducted in Japan (baseline weight 61kg and <6months duration). Compared to control, TZD increased weight by 0.84 kg (95% CI 0.59, 1.09) in these normal weight Japanese subjects. After excluding the outliers, chi-square for heterogeneity was reduced from 184.95 (df=10) to 15.04 (df=6), $p=0.02$.
The pooled analysis found TZDs to induce a weight gain of 3.6 kg or 7.9 lbs (95% CI 3.3, 4.0 kg) over 6 months. There were insufficient data to examine the association between weight gain over time and treatment efficacy (HbA_{1c} reduction) or the effect of different combinations and weight gain.
CONCLUSION: This meta-analysis shows that compared with placebo, TZDs alone or combined to sulfonylureas or metformin results in statistically and clinically significant increase in weight within 6 months of therapy.

86. Evaluation of metformin monitoring in veteran patients undergoing procedures involving non-ionic intravenous contrast dye. *David Parra, Pharm.D., BCPS,* Anna Lindlief, Pharm.D., Nick P. Beckey, Pharm.D., BCPS, Sonia Reyes, R.N., M.S.; West Palm Beach VA Medical Center, West Palm Beach, FL; University of Minnesota, Minneapolis, MN.

PURPOSE: Intravascular radiocontrast studies can lead to acute renal dysfunction and lactic acidosis in patients receiving metformin. It is recommended metformin be withheld 48 hours post-procedure and reinstituted after renal function has been re-evaluated. The objective of this research was to evaluate the efficacy of a computer generated consult in promoting timely evaluation of renal function post-procedure, and measure the incidence and magnitude of serum creatinine elevations.
METHODS: In October 1999 an electronic consult was created for use by the Imaging Service when patients on metformin received intravenous contrast dye. Ordering of the consult generates an electronic notification to a team of pharmacists responsible for providing appropriate follow-up. A retrospective review was done on all consults (118 procedures involving 97 patients) ordered up to January 2002.
RESULTS: One-hundred fourteen of 118 procedures documented the administration of intravenous contrast dye (all non-ionic). Average time from procedure to laboratory follow-up (excluding one patient) was 2.68 ± 1.69 days. Average serum creatinine pre- and post-procedure was 1.10 ± 0.19 mg/dL and 1.12 ± 0.23 mg/dL, respectively ($p>0.05$). Four patients developed contrast-induced nephropathy (increase in serum creatinine of 25%). Serum creatinine was ≥ 1.5 mg/dL in three of these patients, necessitating the temporary discontinuation of metformin. Eight additional patients, with borderline serum creatinine levels at baseline (1.4-1.6 mg/dL), had increases in serum creatinine to 1.5-1.6 mg/dL post procedure, requiring further evaluation of metformin therapy.
CONCLUSIONS: These results indicate that timely follow-up occurs using the combined process of an electronic consult and pharmacists. This study also suggests that nearly 4% of diabetic patients with normal renal function develop contrast-induced nephropathy with non-ionic contrast dye. In addition, about 10% of veteran diabetic patients receiving metformin who undergo a procedure with non-ionic intravenous contrast dye will need to have metformin therapy held beyond 48 hours.

Gastroenterology

87E. Pantoprazole bicarbonate suspension can provide oral bioavailability similar to tablet. Jeffrey Paul, Ph.D., *Geraldine M. Ferron, Pharm.D., Ph.D.,* Sherry Ku, Ph.D., Madelyn Abell, R.N., BSN, Mary Unruh, R.N., MSN, John Getsy, D.M.D., D.O., Philip R. Mayer, Ph.D.; Wyeth-Ayerst Research, St. Davids, PA.

Presented at the 30th International Educational and Scientific Symposium of the Society of Critical Care Medicine, San Francisco, CA, January 22-27, 2001.

88. Esomeprazole capsule contents suspended in water can be efficiently

delivered through nasogastric and gastrostomy tubes. *C. Michael White, Pharm.D.,* James Kalus, Pharm.D., Robert Quercia, M.S., Christopher Fortier, B.S., Alexandria Piotrowski, B.S., Albert Roach, Pharm.D., Mark B. Sostek, M.D.; University of Connecticut, Storrs, CT; Hartford Hospital, Hartford, CT; AstraZeneca LP, Wayne, PA.

PURPOSE: To determine the efficiency of delivery of the contents of an opened capsule of esomeprazole through nasogastric tubes (NGT) and gastrostomy tubes using an in vitro protocol.
METHODS: The percentage of enteric-coated pellets from an opened capsule of esomeprazole 40 mg that passed through either an 8-French NGT, a 14-French NGT or a 20-French gastrostomy tube was measured using 2 methods. In the first, pellets were suspended in 50 mL of tap water in a syringe, injected through the tube, and counted. In the second, pellets were suspended in 25 mL of tap water in a syringe, injected, an additional 25 mL of tap water was washed through the syringe and tube, and pellets were counted. Differences were analyzed using t-tests.
RESULTS: More than 98% of pellets were delivered using the 50 mL method.

	n tubes	Baseline Pellet Count (mean ± SD)	Pellets Delivered Through Tube (mean ± SD)	% Delivery
25 mL + 25 mL method 14-French NGT	5	1242.8 ± 5.6	965.2 ± 87.2	77.7 ± 7.2*
50 mL method				
8-French NGT	5	1244.4 ± 32.9	1219.8 ± 31.4	98.0 ± 1.6
14-French NGT	5	1240.8 ± 19.9	1240.0 ± 20.2	99.9 ± 0.1**
20-French gastrostomy tube	5	1231.8 ± 19.8	1221.2 ± 18.6	99.2 ± 0.5

*P<0.05 versus 14-French NG tube 50 mL method (Student *t*-test); **P<0.05 versus 8-French NG tube (Bonferroni corrected *t*-test)

CONCLUSION: The pellets of an opened capsule of esomeprazole 40 mg suspended in water can be efficiently delivered through an NGT or gastrostomy tube. Administration of an opened esomeprazole capsule through an NGT or gastrostomy tube is likely to be as effective as oral administration in suppressing gastric acid production.

89E. Intestinal P-glycoprotein is important for mucosal defense against *Listeria monocytogenes* infections. *Brien L. Neudeck, Pharm.D.,* Jennifer M. Loeb, B.S., Nancy G. Faith, BMT, Charles J. Czuprynski, Ph.D.; University of Wisconsin, Madison, WI.

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90. Esomeprazole: nasogastric tube administration of the contents of an opened capsule suspended in water compared with oral administration in healthy volunteers. *Mark B. Sostek, M.D.,* Yusong Chen, Ph.D., Wendy Skammer, BSN, Helen Winter, Ph.D., June Zhao, M.D., Tommy Andersson, Ph.D.; AstraZeneca LP, Wayne, PA.

PURPOSE: Nasogastric tube administration of medication may be necessary for patients unable to swallow. Bioavailability of esomeprazole was measured following oral and nasogastric administration.
METHODS: This was an open-label, 2-period crossover study with two 5-day dosing periods separated by a 7- to 14-day washout. Subjects received esomeprazole 40 mg once daily 30 minutes prior to a standardized breakfast in a randomized sequence either orally as an intact capsule (IC) or via syringe through a 16-French nasogastric tube as a suspension of enteric-coated pellets from an opened capsule (OC) in 50 mL water. Following multiple plasma concentration measurements, the AUC and C_{max} for esomeprazole were determined using a one-compartment, open model. Logarithmic values for AUC and C_{max} were analyzed using ANOVA to obtain the least square means of the differences between the OC and IC and the 90% confidence intervals (CI). The antilogarithms of the least square means and the CI were calculated to estimate the ratio of OC/IC and the 90% CI for the ratio.
RESULTS: Geometric means of OC/IC with 90% CI for AUC and C_{max} at days 1 and 5 are presented (table). Similar bioavailabilities between the 2 modes of administration were found.

	N	Ratio (OC/IC) Mean	90% CI
Day 1			
AUC (ng/mL•hour)	47	1.03	(0.93-1.15)
C_{max} (ng/mL)	60	0.87	(0.74-1.02)
Day 5			
AUC (ng/mL•hour)	55	1.14	(1.03-1.26)
C_{max} (ng/mL)	60	1.16	(1.04-1.30)

CONCLUSION: An opened capsule of esomeprazole suspended in water administered via nasogastric tube is a practical alternative for patients unable to swallow the intact capsule.

91E. Lansoprazole fast-disintegrating tablets (15 mg, 30 mg), a new proton pump inhibitor formulation, is bioequivalent to lansoprazole capsules (15 mg, 30 mg). James W. Freston, M.D., Ph.D., Mitchell A. Rosenberg, M.D., Marc A. Saltzman, M.D., *Yi-Lin Chiu, Ph.D.,* David L. Bloom, BGS, Barbara A. Bopp, Ph.D., E. David Ballard, II, M.D.; University of Connecticut Health Center, Farmington, CT; Parkway Research Center, North Miami Beach, FL; Abbott Laboratories, Abbott Park, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL.

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92. Evaluation of a proton pump inhibitor step-down initiative in a Veterans Affairs medical center. *J. Wayne Hamm, Pharm.D.,* Deana M. Washington, Pharm.D., Thomas H. Cobb, Pharm.D., Katherine C. Herndon, Pharm.D., BCPS; Birmingham Veterans Affairs Medical Center; Pfizer Inc., Birmingham, AL.

PURPOSE: A therapeutic interchange was implemented in which patients with a diagnosis of GERD and an active prescription for a proton pump inhibitor (PPI) were converted to ranitidine 300 mg twice daily. This review was designed to compare patients who remained on ranitidine after the therapeutic conversion (non-failure patients) with those patients who were switched back to a PPI in the three months following the intervention (failure patients).
METHODS: Pharmacy records were used to identify failure patients (n=1404) and non-failure patients (n=4639) three months after implementation of the step-down initiative. A random sample of 125 patients was selected from the failure and non-failure groups. A retrospective review of computerized medical and pharmacy records was performed. A binary logistic regression model was used to identify significant predictors of failure.
RESULTS: The mean duration of ranitidine therapy prior to failure was 48.9 ± 24.7 days. Recurrence of symptoms was the most common reason for failure in the first three months after the conversion. Obesity [OR = 2.98; CI, 1.55-5.72] and duration of PPI therapy greater than two years [OR = 3.7; CI, 2.01-6.81] were significant predictors of failing the conversion from a PPI to ranitidine in the three months following implementation of the initiative. Other risk factors for GERD (smoking, hiatal hernia, LESP-lowering medications) did not significantly predict failure.
CONCLUSION: In the three months following implementation of the initiative, obesity and duration of PPI therapy greater than two years were significant predictors of failing the step-down conversion from a PPI to ranitidine.

93E. A prospective, controlled, randomized trial of 3-, 7-, and 10-day rabeprazole-based triple therapy for H. pylori eradication in the U.S. Nimish Vakil, M.D., Howard J. Schwartz, M.D., Frank L. Lanza, M.D., Jay Barth, M.D., *Anita Murthy, Pharm.D.*; University of Wisconsin, Milwaukee, WI; Miami Research Associates, Miami, FL; Houston Institute for Clinical Research, Houston, TX; Eisai, Inc., Teaneck, NJ.

Presented at the Annual Meeting of Digestive Disease Week, San Francisco, CA, May 19-22, 2002.

Geriatrics

94. An evaluation of secondary stroke prevention in elderly long-term care patients. *Bradley E. Hein, Pharm.D.,* Tamara B. Patterson, Pharm.D.; University of Cincinnati; Skilled Care Pharmacy, Cincinnati, OH.

PURPOSE: This study evaluated secondary stroke prevention measures in elderly long-term care patients. As the elderly population increases and there are more stroke survivors, secondary prevention is crucial for both quality of life and economic reasons.
METHODS: Medical records of 418 patients with history of ischemic stroke in 25 Ohio-based nursing facilities were evaluated. Data was collected between June 2001 and December 2001. Data evaluated were the use of antiplatelet/anticoagulant therapy as well as management of stroke risk factors (blood pressure, cholesterol and diabetes, if applicable) in accordance with current practice guidelines. Reasons for not using antiplatelet/anticoagulant therapy in this population were also evaluated.
RESULTS: Antiplatelet/anticoagulant therapy was prescribed for 83% of stroke patients. For stroke patients with atrial fibrillation, antiplatelet/anticoagulant therapy was prescribed 87% of the time. For all patients on warfarin therapy, 52% had an INR 2-3. Blood pressure, cholesterol and diabetes were controlled in 61%, 48%, and 50% of patients, respectively. History of gastrointestinal bleed was the most common reason for not prescribing antiplatelet/anticoagulant therapy.
CONCLUSION: The great majority of stroke patients in our study received secondary prophylaxis, which compares favorably with previously published studies. Risk factor management was suboptimal in certain areas, however. Ongoing clinical trials will help to definitively evaluate the role and outcome of risk factor management in elderly stroke survivors.

95. The impact of an educational intervention on caregiver knowledge of diabetes mellitus in a population-adjusted clinical epidemiology program. *Karen McGee, Pharm.D.,* Tim A. Mullenix, Pharm.D., M.S., Diana Joachim, Pharm.D., Heather Aston, Pharm.D., Janet Thames, Pharm.D.; University of South Carolina; Palmetto Health Alliance, Columbia, SC.

PURPOSE: The purpose of this study was to evaluate the impact of an educational intervention on caregivers of elderly diabetics knowledge about

general principles of Diabetic care practices in a Geriatric Day Health Center.
METHODS: Elderly diabetic patients who take insulin or oral antidiabetic medications for the treatment of DM were identified and informed consent was obtained from their caregivers. The caregivers baseline DM knowledge was then evaluated by administering "The Diabetes Knowledge Test" from the Michigan Diabetes Research and Training Center. An educational program was presented and the caregivers were re-tested.
RESULTS: 80 elderly diabetic patients were identified at Palmetto Senior Care. For the baseline DM knowledge test 47 survey questionnaires were returned by the respective caregivers representing 59% response. After the educational intervention, caregivers were again surveyed with a repeat DM knowledge test and 23 tests were returned representing a 49% response rate of those who received the intervention. The average age for the respondents was 55.8 years and ranged from 28 to 81. 81% of respondents were females and 19% were males. The baseline knowledge score average was 11.1 (48.2%) and ranged from 6 (26%) to 19 (83%). The reevaluation knowledge score average was 17.8 (77.5%) and ranged from 9 (39%) to 23 (100%). The difference between the percent correct post test and baseline evaluation was significantly different using a 2-sample t-test with $p<0.001$ (CI of 20.2, 38.5).
CONCLUSIONS: Baseline DM knowledge scores for caregivers of elderly diabetic patients were generally low. An educational intervention provided by a clinical pharmacist significantly improved DM knowledge scores in these caregivers.

96. A randomized clinical trial of functional assessment and medication management in community-dwelling elders. Mark E. Williams, M.D., *Charles C. Pulliam, M.S., Pharm.D.*, Rebecca Hunter, Theodore M. Johnson, M.D., Justine E. Owens, Ph.D., Jean Kincaid, Ph.D., Carol Porter, M.S., Gary G. Koch, Ph.D.; University of Virginia, Charlottesville, VA; Virginia Commonwealth University, Richmond, VA; University of North Carolina, Chapel Hill, NC; Emory University, Atlanta, GA.

PURPOSE: The study objective was to measure the effect of regimen changes instituted by a specialized geriatric assessment team on medication cost and physical, cognitive and affective functioning of elders taking multiple medications.
METHODS: 133 community-dwelling elders (63 intervention subjects; 77 controls) taking five or more medications participated. Drug regimens of intervention elders were modified following a comprehensive review; both groups were assessed at baseline and 6 weeks. Measures of function included [*Physical*] Timed Manual Performance (TMP) Test, Physical Performance Test (PPT), and Functional Reach Assessment (FRA); [*Cognitive*] sub-tests from the Wechsler Adult Intelligence Scale (WAIS-R) and a modified Randt Memory Test; [*Affective*] the Center for Epidemiological Studies-Depression Scale (CES-D) and the Self-Rating Anxiety Scale (SAS); and [*Health Status*] the Rand 36-item Health Survey 1.0. Comorbidity was determined by ICD-9-CM and *Medication Usage* by "brown bag" review.
RESULTS: Intervention subjects decreased their medications by an average of 1.5 drugs. No adverse events resulted from the medication adjustments and no significant differences in physical, cognitive or affective functioning were observed between intervention and control subjects. Financial analysis revealed that intervention subjects saved an average $26.92 per month in medication costs; control subjects saved $6.75 per month ($p<0.006$). Had all recommendations been followed, intervention subjects would have saved $96.36 per month.
CONCLUSION: Medication adjustment can be safely performed in an outpatient setting with minimal initial impact on function or quality of life. While the intervention was effective in significantly reducing medications use and cost, most patients taking five or more prescription drugs were resistant to reducing medication consumption to recommended levels.

97. Reduction by olanzapine of occupational disruptiveness among caregivers of patients with Alzheimer's dementia. *Peter D. Feldman, Ph.D.*, John S. Kennedy, M.D., Carrie A. Young, M.Sc., Deborah L. Kadam, M.A., Willie R. Earley, M.D., Alan Breier, M.D.; Lilly Research Laboratories, Indianapolis, IN.

Neuropsychiatric disturbances in patients with dementia can impact caregivers and affect overall patient management.
This *a priori*-defined analysis investigates changes in caregiver distress, as measured by Occupational Disruptiveness scores associated with each individual dimension of the Neuropsychiatric Inventory–Nursing Home version (NPI/NH) rating scale. Elderly nursing-home patients with Alzheimer's dementia were randomized to either placebo or fixed-dose olanzapine (Olz: 5, 10, or 15 mg/day) for 6 weeks of double-blind therapy. Successful completers entered an 18-week open-label extension, during which they received flexible-dose Olz (5–15 mg/day).
After the acute phase, reductions were seen in distress ratings reported by caregivers of patients receiving low-dose (5 mg) Olz. Significant reductions occurred relative to placebo in the NPI/NH Occupational Disruptiveness Psychosis Total (sum of *Hallucinations* and *Delusions* scores) and Core Total (sum of *Hallucinations*, *Delusions*, and *Agitation* scores) scores, and in the *Delusions* and *Irritability* dimensions. Results with higher doses (10, 15 mg) were largely nonsignificant compared to placebo. However, patients entering the extension improved significantly further on the Occupational Disruptiveness total, Psychosis Total, and Core Total, and in the *Agitation*, *Delusions*, *Disinhibition*, and *Irritability* dimensions.
These results indicate that olanzapine may significantly reduce occupational disruptiveness for caregivers of dementia patients with neuropsychiatric disturbances.

98. Patterns of anti-osteoporotic drug use among older community dwelling west Texans and associated factors. *Carlos H. Rojas-Fernandez, Pharm.D.*, Kellee A. Howard, M.A., M.S., Niti Goel, M.D.; Texas Tech University Health Sciences Center, Amarillo, TX; Procter & Gamble Pharma, Galveston, TX.

PURPOSE: Emerging evidence suggests that osteoporosis (OP) is under-treated in older (≥ 65 years) people. There are no data however, that describe anti-osteoporotic (AOP) drug use in older people living in rural areas. The purpose of the present study is to; 1) to describe AOP drug use among community dwelling older people living in West Texas and, 2) to assess whether factors related with accessibility to health care or sociodemographic factors affect rates of AOP drug use in this population.
METHODS: This was a cross-sectional telephone survey using the Texas Tech 5000 (TT5000) survey data set as the sampling frame. The TT5000 was a survey designed to collect health status and service information from 5000 older people living in the 108 counties that comprise West Texas. Random digit dialing was used to select the study sample. To date, two waves have been conducted: the first two waves were completed in the fall 2000 and spring of 2001. These were designed to collect baseline information regarding health care status, health care utilization, functional status, disease state information, information regarding medication use, as well as demographic information. Subjects who responded as having been diagnosed with OP or osteopenia (OPE) in the second wave were selected for the present study. A questionnaire (which was pre-tested) was developed to collect information regarding the subject's self-reported diagnoses of OPE or OP, as well how the diagnosis was established and current AOP drug use which was administered over the telephone by trained interviewers. Data from the present survey [data collection completed in March 2002] was linked with data from the previous TT5000 survey waves. The SPSS statistical software package was used for analyses.
RESULTS: In the TT5000, 744 subjects indicated that they had OP or OPE, 555 of which participated in the present study and are thus compose the study sample (the remaining 25% refused or were lost to follow up). A diagnosis of OP was reported by 72%, while a diagnosis of OPE was reported by 11%. Overall, 63% were aged 65-75 years, 37% were ≥ 76 years, and 93% were female. The types and frequencies of medications which were reported by the subjects were as follows: bisphosphonates (27%), raloxifene (7%), calcitonin (5%), estrogens (28%) and calcium or calcium & vitamin D products (100%). The proportion of subjects with OP who reported taking drugs that are FDA-approved for the treatment of OP was 43%. Analyses to assess the effects of ; a) factors related to accessibility for health care and, b) sociodemographic factors, on the rates of AOP drug use in this population are currently ongoing.
CONCLUSIONS: The present data suggest that an important proportion of older people with OP are not receiving drugs that are FDA approved for the treatment of OP, but rather are only receiving preventative therapy. Further research is necessary to clarify reasons for these findings.

99. Does a clinical pharmacist visit improve patient drug knowledge in the elderly? *Cynthia K. Schulte, Pharm.D. candidate*, Angela B. Hoth, Pharm.D., Peter J. Kaboli, M.D.; Iowa City VAMC; University of Iowa, Iowa City, IA.

PURPOSE: To determine if a clinical pharmacist evaluation is associated with increased patient knowledge of drug indication.
METHODS: The study population included 159 cognitively intact patients ≥ 65 years of age and prescribed ≥ 5 scheduled medications in a VA primary care clinic from 7/01-2/02. Randomized subjects received usual care (control) or usual care plus a clinical pharmacist evaluation (intervention). Subjects stated from memory the indication for each of their medications at baseline and 3-month follow-up interviews. Medical records were used to verify response correctness. The change in knowledge from baseline to 3-months was compared between the intervention and control groups.
RESULTS: 76 intervention and 83 control patients averaged 74 years of age, were 98% male, 98% white, and 58% completed high school. No differences existed between the groups with regard to age, sex, race, or level of education ($p>0.1$). At baseline, intervention patients reported taking a mean of 12.5 ± 4.1 medications and controls 11.2 ± 4.0 ($p=0.05$). The mean percentage of drug indications known was 75% for interventions and 72% for controls ($p=0.55$). At 3-month follow-up, intervention patients reported taking 12.0 ± 4.2 medications and controls 11.5 ± 4.1 ($p=0.45$). Drug indication knowledge remained steady in the intervention group at 75%, but decreased to 64% in the control group ($p=0.03$).
CONCLUSIONS: A clinical pharmacist visit was associated with maintenance of patient knowledge of drug indication. Control patients who did not meet with a pharmacist had a significant decrease in knowledge compared to the intervention group.

100. Assessment of factors impacting medication adherence among community-dwelling older adults. *Martin R. Giannamore, Pharm.D., BCPS*, Laura L. Manzey, Pharm.D., BCPP, Margaret A. Olmon, R.Ph., M.B.A., Kevin A. Townsend, Pharm.D., BCPS; Pfizer Inc., Cleveland, OH.

PURPOSE: Medication adherence scores were evaluated in community-dwelling older adults to determine if a relationship existed between medication adherence and educational level, income, number of medical conditions, number of prescription medications, and receipt of pharmacist counseling.
METHODS: Surveys were analyzed from 113 older adults who voluntarily attended medication management seminars at area senior citizen centers between August 9 and October 24, 2001. A four-question, self-reported medication adherence measurement (designed by Morisky, et al) was included in the survey. Adherence scores were categorized as "high", "medium", or "low" based upon the total score for each respondent. The Chi-Square Test of Independence was utilized for statistical analysis.
RESULTS: The population was comprised of mostly Caucasian (79%) females (76%) aged 76 years (mean) with either a high school (67%) or college (20%) education. Adherence scores for 95 of the respondents were categorized as follows: "high" in 47 (50%) respondents, "medium" in 44 (46%) respondents, and "low" in 4 (4%) respondents. No relationship existed between adherence score category and any of the following: mean number of medical conditions, mean number of prescription medications, and income level. Trends toward improved adherence scores among respondents with a higher educational level and positive recall of pharmacist counseling existed, but these were not statistically significant.
CONCLUSIONS: Findings demonstrating no relationship between medication adherence and the variables studied may have been due to insufficient sample size and selection bias. The trend toward adherence score differences based on educational level and receipt of pharmacist counseling will be evaluated through future research and intervention programs in this population.

101. The relationship of an anticholinergic rating scale with serum anticholinergic activity in elderly nursing home residents. *Ryan M. Carnahan, Pharm.D.*, Brian C. Lund, Pharm.D., M.S., BCCP, Paul J. Perry, Ph.D., BCCP, Kennith R. Culp, Ph.D., R.N.; University of Iowa, Iowa City, IA.

PURPOSE: To use serum anticholinergic activity (SAA) to assess the validity of a modified version of the clinician-rated anticholinergic scale (CR-ACh-mod) in assessing anticholinergic medication exposure.
METHODS: Subjects were part of a study of delirium in elderly residents of rural long-term care facilities. Medication regimens for assessment were from taken from a baseline time-point and included prn medications if they were administered the day before blood was drawn to measure SAA. Blood was drawn on day 14 of the study and SAA was measured by radioreceptor assay. Anticholinergic medication exposure was quantified with the CR-ACh-mod. This scale assigns a value of 0 (none) to 3 (marked anticholinergic effects) to each drug in a subject's drug regimen and sums the values to create the CR-ACh-mod score.
RESULTS: The population of 96 subjects had a mean ± SD age of 87 ± 7 years (range 68-106) and 82.3% were female. The mean ± SD SAA was 0.91 ± 0.51 pmol atropine equivalents (range 0.09-2.61). The mean ± SD CR-ACh-mod score was 2.8 ± 2.3 (range 0-9). CR-ACh-mod scores were significantly associated with SAA using linear regression ($t=2.68$, 1 df, $p=0.0087$). However, the scores only explained 7.1% of the variance in SAA, suggesting that improvements in the CR-ACh-mod may increase its robustness as a measure of anticholinergic exposure.
CONCLUSIONS: These findings help support the validity of the CR-ACh-mod. However, unexplained variance in SAA suggests that the CR-ACh-mod could benefit from improvements. Future research will evaluate the effect of including factors such as dose. An alternative explanation supported by recent research is that non-drug factors contribute to SAA.

102. Evolution of antidepressant's use in elderly. *Caroline Trivin*, Laurent Amico, M.D., Benoit Allenet, Pharm.D., Jean Calop, Pharm.D., Alain Franco, M.D.; Center Hospital at the University of Grenoble, Grenoble, France.

PURPOSE: Although depression states in the elderly are frequent, their diagnosis is often difficult and that is why antidepressant drugs are insufficiently used. Because drug therapy of depression evolved very much these years (e.g., new medicines, widest therapeutic indications), we thought it was interesting to take stock of antidepressant prescription in elderly people.
METHODS: A study in a geriatric care unit: One month prospective study, 231 prescriptions analyzed.
RESULTS: Antidepressant were prescribed in 36% of the patients and 57% of them received also hypnotic and sedative drugs. Most of antidepressants were selective serotonin reuptake inhibitor (46.5%): paroxetine (39.3%), fluoxetine (3.6%), citalopram (3.6%). The other molecules prescribed were tianeptine (21.4%), mianserin (14.3%), venlafaxine (14.3%), viloxazine(3.5%). Analysis of the posology showed that guidelines for antidepressant prescription in elderly people were abided, in particular the precaution of use induced by pharmacokinetics modifications due to ageing.
CONCLUSIONS: The use of Monoamine oxydase inhibitor has significantly declined: contraindications and risks are important and their prescriptions have to be well advised and restricted. At present, tricyclic antidepressant's indications are mainly the treatment of neurogenic pains. Our study showed that selective serotonin reuptake inhibitor (SSRI) are widely prescribed and we can explain it by their effectiveness and their facilities of use (low toxicity and large therapeutic safety margin). However we must be aware that use of SSRI is not without risks, adverse effects such as hyponatremia or serotoninergic syndrome can occur, and of course there are possibilities of drug interactions. Drug therapy is necessary and important in the management of depression; nevertheless we have to remember the psychotherapeutic aspect of the treatment.

103E. Effect of proton pump inhibition on 45-calcium carbonate absorption. *Mary Beth O'Connell, Pharm.D., BCPS*, Denyse Madden, Pharm.D., Anne Murray, M.D., Robert P. Heaney, M.D., Lawrence J. Kerzner, M.D.; Wayne State University, Detroit, MI; University of Minnesota, Minneapolis, MN; Walgreens Pharmacy, Woodbury, MN; Hennepin County Medical Center, Minneapolis, MN; Creighton University, Omaha, NE.

Presented at the Annual Meeting of the American Geriatrics Society, Washington, D.C., May 10, 2002.

104. The impact of telepharmacy on medication appropriateness and untreated conditions in elderly veterans. *Sallie D. Mayer, Pharm.D., M.B.A.*, Christine M. Ruby, Pharm.D., BCPS, Benita E. Busch, Pharm.D., Jack I. Twersky, M.D.; Veterans Affairs Medical Center, Durham, NC; Duke University Medical Center, Durham, NC; University of North Carolina, Chapel Hill, NC.

PURPOSE: This study described outcomes utilizing telepharmacy, an innovative approach to providing pharmaceutical care to patients at a distance, in order to: 1) determine if a clinical pharmacist using a telemonitor and interacting with the members of the telehomecare team could improve suboptimal prescribing, and 2) document the acceptance rate of clinical pharmacist recommendations.
METHODS: Ten elderly frail ambulatory veterans who had made six or more visits to the emergency department the preceding year and live > 35 miles from the facility were enrolled from November 2001 to February 2002. Telemonitors were placed in patient homes and a medication history documented. Suboptimal prescribing was assessed at baseline and closeout four weeks later using the Medication Appropriateness Index (MAI) and the Assessment of Underutilization (AOU) tools. Patients were contacted via the telemonitor every one to two weeks. All clinical pharmacy interventions were documented.
RESULTS: There was a slight increase in the number of medications from baseline to closeout although the appropriateness of these medications (as indicated by the MAI score) improved significantly ($p<0.03$). The number of untreated conditions trended toward improvement but was not statistically significant ($p=0.25$). The acceptance rate for clinical pharmacy recommendations was 71% overall (65% for therapeutic and 91% for lab/monitoring recommendations) at closeout.
CONCLUSION: Medication appropriateness improved significantly and untreated conditions trended toward improvement during the study period. Our results indicate that telepharmacy is a useful means to provide clinical pharmacy services. A clinical pharmacist working on a geriatric interdisciplinary telehomecare team can improve suboptimal prescribing.

105. The effect of telepharmacy on elderly veteran medication compliance and patient satisfaction. *Benita E. Busch, Pharm.D.*, Christine M. Ruby, Pharm.D., BCPS, Sallie D. Mayer, Pharm.D., M.B.A., Jack I. Twersky, M.D.; Veterans Affairs Medical Center, Durham, NC; Duke University Medical Center, Durham, NC; University of North Carolina, Chapel Hill, NC.

PURPOSE: This study described outcomes utilizing telepharmacy, an innovative approach to providing pharmaceutical care to patients at a distance, in order to: 1) determine if a clinical pharmacist using a telemonitor and interacting with the members of the telehomecare team could improve patient compliance and knowledge, and 2) describe patient satisfaction with telehomecare technology and the pharmacist.
METHODS: Ten elderly veteran patients determined to be high emergency room users (≥ 6 in past year) and meeting criteria for frailty were enrolled in the telemedicine study. During the initial home visit to set up the telemonitor, the pharmacist obtained a complete medication history and assessed the patient/caregiver baseline knowledge and compliance. Baseline satisfaction with the use of telehomecare technology was assessed during the first telepharmacy visit. Closeout assessment was compared with baseline data. Pharmacist satisfaction with the use of technology was also reported.
RESULTS: Medication Compliance (Admission 62.6% ± 16.7, Closeout 80.8% ± 8.6) improved significantly ($p=0.008$). Knowledge showed improvement, but was not significant. Patient satisfaction with technology was high at baseline (mean summated score 22.4, range 19-25) and remained so at study closeout (mean summated score 24.3, range 23-25). Pharmacist satisfaction with the telemonitors was also high (mean summated score 26.5 out of possible 35).

CONCLUSION: Telepharmacy improves medication compliance in an elderly veteran population and satisfaction with the technology remained high throughout the study. This is a new health care model for delivery of pharmaceutical care to elderly patients at a distance.

106E. Multi-center, open label, naturalistic study of mirtazapine orally disintegrating tablets in depressed nursing home patients. *Steven P. Roose, M.D.,* J. Craig Nelson, M.D., Carl Salzman, M.D., Steven B. Hollander, M.D., James V. Betzel; Columbia University, New York, NY; Yale University, New Haven, CT; Massachusetts Mental Health Center, Boston, MA; Organon Pharmaceuticals Inc., West Orange, NJ.

Presented at the 32nd Annual Meeting of the American Society of Consultant Pharmacists, Chicago, IL, November 7-10, 2001.

107E. Risperidone in treating agitation and psychosis associated with dementia. Alistair Burns, M.D., Grant Ko, M.D., *Fred Grossman, D.O.*; Wythenshawe Hospital, Manchester, United Kingdom; Johnson & Johnson Pharmaceutical Research & Development, LLC, Titusville, NJ.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Pharmacologicum, Montreal, Canada, June 23-27, 2002.

108. Evaluation of effectiveness of alendronate and calcitonin in reducing fractures in a nursing home. *Shyam D. Karki, Pharm.D.,* Christopher Wallace, Pharm.D.; University at Buffalo, Buffalo, NY; Monroe Community Hospital, Rochester, NY.

Nursing home residents fall frequently and some of them result in fractures often needing hospitalizations and prolonged rehabilitation. Even then, most of the residents never regain their prior level of functioning. Osteoporosis has been associated with many fractures in the nursing home and two medications; alendronate (A) and calcitonin (C) have been used to prevent further progression of osteoporosis and thus reduce the number of fractures in this population. This study looks at the fractures in this population in 1 year before and 1 year after initiation of A & C.
Residents on A & C therapies were identified through Pharmacy records and their charts were retrospectively reviewed for number of falls and fractures during the study period. The number of falls and fractures were corroborated with incident reports.
There were 25 residents on A and 24 residents on C. Residents on A had 34 falls during the year before and 36 falls during the year after its initiation. They had 13 fractures before and 0 after the initiation. Residents on C had 52 falls before and 45 falls after its initiation. There were 13 fractures before and 3 fractures after its initiation.
Results were analyzed by Chi Square test and no statistically significant differences were found in falls before and after the initiation of A or C. There was a statistically significant difference in number of fractures before and after initiation of both A & C.
Our results indicate the effectiveness of alendronate and calcitonin in reducing fractures in nursing home population with osteoporosis.

109. The evaluation of pain and depression in the elderly. Carla A. Zeilmann, Pharm.D., BCPS; St. Louis College of Pharmacy, St. Louis MO

PURPOSE: This evaluation was conducted to examine how often patients' self-reporting of pain or depression were addressed by physicians in an academic VAMC geriatric clinic.
METHODS: While waiting to see the physician, each patient completes a brief 4-item self-rated pain, depression, and quality of life inventory. Patients present the completed inventory to the physician at the beginning of each clinic visit. Data for this cross-sectional evaluation were collected from 100 consecutive outpatient visits in March 2002.
RESULTS: Forty-two of the 100 patients answered the question about being in pain positively, and 12 answered the question about feeling sad, blue or depressed positively. The median level of pain for patients expressing pain was 3 (range 1-10 on a 10-point scale). Of the 42 patients reporting pain, 19 physicians' progress notes included pain as a problem discussed during the visit; and action, in the form of non-pharmacologic therapy, a new prescription or consult to a specialist, was taken on 11 patients. The median level of pain for a patient the physician included in the note or acted on was 4 (range 1-10). Of the 12 patients stating they felt depressed, 7 physicians' notes included depression as a problem, and 4 noted action in the form of a new prescription or consult to psychiatry.
CONCLUSIONS: Approximately one-quarter of patients reporting pain and one-third of patients reporting symptoms of depression received new therapy for these problems. More effort should be extended to address and treat these disorders in this geriatric population.

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110. A measurement tool for physician/pharmacist collaboration. *Alan J. Zillich, Pharm.D.,* William R. Doucette, Ph.D., Barry L. Carter, Pharm.D., BCPS, FCCP; University of, Iowa City, IA.

PURPOSE: Recently, a conceptual behavioral framework has been conceived which categorizes a hierarchy of collaboration between the physician and pharmacist. However, there is no easy method for measuring collaboration. Consequently, we developed a survey tool to elicit the degree of collaboration that occurs between physicians and pharmacists. Using the behavioral framework, a 27-item questionnaire was developed and pilot-tested for reliability and validity.
METHODS: The instrument contains 8 domains (Collaborative Care, Commitment, Scope of Relations, Dependence Symmetry, Bi-Directional Communication, Trust, Initiating Behavior, and Conflict Resolution) measured with a 7-point Likert scale. Twenty-one Family Medicine physicians at a large University outpatient clinic were asked to complete this questionnaire along with a previously validated measure of collaboration, at two time points separated by a 2-4 week interval. Cronbach's alpha and Pearson's correlation coefficients were calculated for reliability and inter-item correlation. Construct validity and test/re-test reliability were assessed using Pearson's correlations.
RESULTS: Seventeen physicians completed the initial survey with 11 completing the retest. Cronbach's alpha ranged from 0.619 to 0.925 among the domains. All inter-item correlations were statistically significant ($p \leq 0.05$). Collaboration domain correlations between the two instruments were significant ($r=0.756$, $p=0.01$). The other domain scales showed similar significant correlations between surveys. Test/Re-test correlation coefficients were in the expected direction for all domains and statistically significant in 4 of the 7 domains ($p=0.01$).
CONCLUSION: Results from this initial pilot-study indicate strong reliability and inter-item correlation for this instrument. Further research is needed to evaluate this measurement tool.

111. Treatment adequacy with venlafaxine extended-release or fluoxetine. Kristina Yu-Isenberg, Ph.D., M.P.H., R.Ph., Christina Fontes, *George J. Wan, Ph.D., M.P.H.,* Erika C. Geissler, R.N., M.B.A.; Prescription Solutions, Costa Mesa, CA; Wyeth Research, St. Davids, PA.

PURPOSE: This study examined treatment adequacy with venlafaxine extended-release (VENXR) or fluoxetine in a managed care setting.
METHODS: A retrospective pharmacy claims analysis was performed using data from Prescription Solutions. Treatment adequacy was defined using the HEDIS Antidepressant Medication Management measures for continuous therapy for 84 or 180 days at the target dose (75-150 mg/day for VENXR; 20 mg/day for fluoxetine). Pharmacy claims were obtained for 90 days prior and 270 days after the index prescription for either VENXR or fluoxetine during the index period (01/01/00-02/28/01). The cohort included patients newly starting with either VENXR or fluoxetine and remaining on the same medication for 84 or 180 continuous days. Logistic regression was used to evaluate the impact of VENXR or fluoxetine on treatment adequacy controlling for age, gender, prescribing physician, and pharmacy benefit type.
RESULTS: VENXR ($n=1591$) had an adequacy rate of 79% compared to 57% for fluoxetine ($n=3389$) for 84 continuous days ($p<0.0001$). VENXR ($n=1054$) had an adequacy rate of 77% compared to 52% for fluoxetine ($n=2251$) for 180 continuous days ($p<0.0001$). The adjusted odds ratios (OR) of achieving treatment adequacy with VENXR versus fluoxetine were 3.05 (95% CI=2.65-3.52) for 84 continuous days and 3.57 (95% CI=3.00-4.24) for 180 continuous days.
CONCLUSIONS: Patients prescribed VENXR achieved higher treatment adequacy rates compared to fluoxetine. Patients taking VENXR were three times more likely to achieve treatment adequacy than fluoxetine. Treatment adequacy as a proxy for optimal treatment may be an important factor to consider when selecting antidepressant medication.

112. Decentralized pharmacy technicians: a novel role for the pharmacy technicians in drug distribution and cost contaminant. *Shewan M. Aziz, R.Ph., Ph.D., BCOP,* Dana Hunter, R.Ph., Angela Hollis-Dumas, C.Ph.T., David Crabtree, C.Ph.T., M.S., James A. Raczek, M.D.; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: A trial of decentralized pharmacy technicians on one of our inpatient floors was conducted to examine the impact of this novel program on the efficiency of drug distribution, quality of patient care, clinical pharmacy practice, nursing relations, medication utilization and cost, Pyxis overrides, medication charging process, nursing time, and job satisfaction.
METHODS: Nationally certified pharmacy technicians with several years of experience were selected to be the nucleus of this program. The technicians received further training from our clinical pharmacists and clinical pharmacy informatics technician on how to collect and tabulate clinical data. The technicians also completed and demonstrated competency in communications and nursing relations through courses provided by the Department of Education. One medical floor was selected for the decentralized technicians trial based on the high patient volume, number of medication doses dispensed, drug distribution issues, and communication issues. Decentralized technicians were available on the floor for 16 hours/day for 7 days/week and could be reached by their pagers. Technicians were assigned primary distribution duties along with secondary duties as determined by the needs of the floor. A centralized pharmacy technician was assigned the duties of

picking IV and oral medications for the decentralized technicians to further enhance the medication turn around time (TAT). To organize the decentralized technicians daily functions the following daily reports were generated, a list of patients without height (HT), weight (WT), or allergy information, patients with active PCA/epidural orders, and patients on IV medications listed in the IV to PO autosubstitution program. In addition, the technicians monitored medications ordered but not verified by pharmacists and created an on time daily transfer list to assure that medications are transferred with the patients.
RESULTS: Data to measure the effectiveness of the program was collected. There was a significant decrease in the number of phone calls to the pharmacy regarding missing medication from the unit. There was a decrease in TAT of medications (emergency, stat, and drug ordered but not loaded in Pyxis). The reduction in TAT significantly reduced the number of medication overrides performed in Pyxis by nurses on that floor. There was improvement in maintenance of Pyxis machines. There was better management of outdated and expired drugs. There was considerable savings in medication cost because of the decentralized technicians tracking medication use, crediting outdated, expired, and returned medications, reusing of expensive medications (Epogen, Lovenox, ointments, inhalers, eye drops), reducing IV wastes, and providing the pharmacists with a list of patients on IV medications eligible for oral conversation. The efficient removal of outdated and expired IV medications from the floor also reduces the potential for medication errors. Our nursing and technician survey data showed a tremendous increase in satisfaction from both sides and an actual decrease in nursing time and overtime used to track missing medications or to correct Pyxis malfunction. In addition to the results mentioned above, the focus of our staff pharmacists has shifted from dealing with drug distribution issues to providing clinical pharmacy services. The availability of HT, WT, and allergy information provided by the technicians increased the performance of the Cerner® software available in Pharmacy computer system. This software was programmed to detect and alert pharmacists performing order entry to potential adverse drug events due to inappropriate drug dosage or organ dysfunction.
CONCLUSION: The implementation of this program was a great success in regard to improved patient care, nursing relations, clinical activities, job satisfaction, and reduced medication errors and cost. Accordingly, this program was expanded to include all of our inpatient care areas. We will continue to evaluate the current activities and consider new activities, such as involving our technicians in collecting pharmacokinetic data to monitor the use of high-risk drugs. We recently added the tracking of automatic stop order notifications for drug renewal as an additional task for this program.

113. Prevalence of the metabolic syndrome in the southwestern United States. *William D. Linn, Pharm.D.*, Thomas C. Shank, Pharm.D.; University of Texas; Pfizer Pharmaceuticals, San Antonio, TX.

PURPOSE: Recent NHANES data has reported that the prevalence of the metabolic syndrome is high in US adults. This study assessed the prevalence of this syndrome in a large urban area in the Southwest.
METHODS: A citywide cardiovascular screening was held in San Antonio, Texas in December 2001. A complete data set was available for 9287 adults 20 years and older. A metabolic syndrome was defined as at least 3 of the following: triglycerides (TG) ≥ 150 mg/dL; a high-density lipoprotein cholesterol (HDL-C) level < 40 mg/dL in men or < 50 mg/dL in women; a blood pressure (BP) of at least 130/85 mm Hg; or a serum glucose level of at least 110 mg/dL.
RESULTS: The prevalence of the metabolic syndrome for the Non-Hispanic cohort was 25.6%. The most common combination was TG, HDL-C, and BP. The Hispanic population had an increased rate at 30.4%. Among the Hispanic population, men were more likely to have a metabolic syndrome than women with rates of 34% and 28% respectively.
CONCLUSION: These data are concordant with the NHANES data except that the current rates are higher than the 21.8% reported in 1988 to 1994. This could represent the increasing levels of obesity in the US or that this geographic area has higher rates of the metabolic syndrome compared to other areas in the US. Healthcare costs related to the metabolic syndrome are tremendous. All healthcare professionals need to aggressively council patients on dietary modifications, increased physical activity, and weight loss.

114. Community screening for diabetes: should demographics be a factor? *William D. Linn, Pharm.D.*, Thomas C. Shank, Pharm.D.; University of Texas; Pfizer Pharmaceuticals, San Antonio, TX.

PURPOSE: The U.S. Preventive Services Task Force does not recommend routine screening for type 2 diabetes and the ADA guidelines recommends screening only under certain circumstances such as having a positive family history or being of certain ethnic backgrounds. This study looks at a large community-screening project in a predominantly Hispanic population.
METHODS: A citywide screening was held in San Antonio, Texas during December 2001. Data collected included demographics, medical history, vital signs, a full lipid profile, and a fasting or random glucose.
RESULTS: A complete data set was available for 4231 males and 5339 females. Sixty two percent were Hispanic. Fifty one percent of males had a Body Mass Index (BMI) > 27 compared to 49% of females. Two percent of males and 1% of females had a random glucose (RG) > 140 mg/dL but 27% and 23% respectively, had reported fasting glucose values > 110 mg/dL. For Non-Hispanics, 8% of males and 11% of females were significantly obese (BMI > 35) compared to 12% and 17% for Hispanics. Of these, 43% of non-Hispanic males and 25% of non-Hispanic females had glucose intolerance compared to 40% and 35% for Hispanics respectively.
CONCLUSIONS: Despite recommendations against community screening for diabetes, certain cities or populations might still benefit. Pharmacists are frequently involved in these activities and should understand the significance of who would benefit the most from screening programs. Being obese, especially for Hispanic females, warrants screening. This project identified several hundred people needing aggressive lifestyle modification and/or drug therapy.

115. Impact of a collaborative care model for depression in primary care: a randomized controlled trial. *Patrick R. Finley, Pharm.D., BCPP,* Heidi R. Rens, Pharm.D., Joan T. Pont, M.D., Clifton Louie, D.P.A., Susan L. Gess, Pharm.D., Scott A. Bull, Janelle Y. Lee, Ph.D., Lisa Bero, Ph.D.; University of California, San Francisco, CA; Kaiser Permanente, San Rafael, CA; Alza Pharmaceuticals, Mountain View, CA; Kaiser Permanente, Oakland, CA.

PURPOSE: Preliminary research suggests that clinical pharmacists may have a favorable impact upon depressed patients in primary care. The objective of this investigation was to evaluate the clinical and economic impact of pharmacists under the rigor of a randomized controlled trial.
METHODS: Patients were randomized to the investigation immediately after initiation of an antidepressant. The intervention group received medication management and follow-up services from clinical pharmacists through scheduled clinic visits and telephone contacts while the control group was managed by the referring physician (i.e., usual care). Medication adherence and resource utilization were determined from the HMO's electronic medical information system. Clinical outcomes and patient satisfaction were compared from surveys mailed six months after randomization.
RESULTS: An intent-to-treat analysis revealed that 68% of the intervention group (n=75) and 52% of the control group (n=50) completed six months of antidepressant treatment (p=0.072; OR = 1.96, 95% CI 0.88-4.39) and switch rates were higher as well (19% vs. 4%; p=0.016). Clinical and functional outcomes were similar. Patient satisfaction was greater among the patients receiving collaborative care, specifically in regard to the HMO, overall treatment, personal nature and access to care (p<0.05 all measures). Provider satisfaction scores were also favorable. Total resource utilization was similar between groups but there was a significant decline in primary care visits with the intervention group (39% decrease vs. 1% increase; p=0.015).
CONCLUSIONS: Results of this investigation provide further evidence that direct involvement of clinical pharmacists in the management of depressed patients can improve outcomes and satisfaction. Studies of this treatment model in different health care settings appear warranted.

Hematology/Anticoagulation

116. Association between renal dysfunction and bleeding in low molecular weight heparin-treated patients. *Carl W. Peterson, Pharm.D.*, Amy E. Jackson, Charlie W. Ham, Pharm.D.; Cardinal Health Provider Pharmacy Services, Punta Gorda, FL, and Houston, TX.

PURPOSE: Evaluate the relationship between renal dysfunction and bleeding in patients receiving low molecular weight heparin (LMWH) prophylaxis or treatment.
METHODS: Medical records of 1079 consecutive patients treated with LMWH between January and March 2001 at 24 hospitals were reviewed. Age, sex, height, weight, serum creatinine, LMWH dose, indication, and in-hospital clinical and bleeding outcomes were documented. Standard bleeding definitions were used. Creatinine clearance (ClCr) was calculated using the Cockroft/Gault formula. Incidence of major and minor bleeding was determined in patients with ClCr > 30 ml/min (NRF) and ≤ 30 ml/min (RF). Fisher's exact test was used for statistical analysis.
RESULTS: Of 817 patients in whom ClCr could be calculated, 43 (13.4%) of 320 prophylaxis and 81 (16.3%) of 497 treatment patients had ClCr ≤ 30 ml/min. Mean dose was similar in the NRF and RF groups for both prophylaxis and treatment (weight-adjusted). In the prophylaxis group, overall bleeding incidence was similar between the RF and NRF groups (overall 11.6% vs. 7.2% respectively, p=0.36) (major bleeding 4.7% vs. 5.1%, minor bleeding 7.0% vs. 2.2%). In the treatment group, overall bleeding incidence was greater in RF than NRF (overall 9.9% vs. 3.4% respectively, p=0.016) (major bleeding 6.2% vs. 1.7%, minor bleeding 3.7% vs. 1.7%). The difference in treatment group major bleeding was significant, p=0.03.
CONCLUSIONS: Major bleeds were significantly more frequent in the RF treatment group. Renal dysfunction appears to be associated with increased bleeding risk in LMWH-treated patients.

117. Retrospective evaluation of vitamin K_1 usage to reverse the anticoagulant effect of warfarin. *Jingyang Fan, Pharm.D.*, John A. Armitstead,

M.S., FASHP, Aimee G. Adams, Pharm.D., George A. Davis, Pharm.D.; University of Kentucky, Lexington, KY.

PURPOSE: This retrospective study was designed to 1) assess compliance with the 2001 American College of Chest Physicians (ACCP) consensus guidelines on the use of vitamin K_1 for reversal of the anticoagulant effect of warfarin, and 2) determine physician preference in route and dose of vitamin K_1 in a university hospital setting.
METHODS: Medical records of 56 adult inpatients who received both warfarin and vitamin K_1 were evaluated. Patient demographic information, vitamin K_1 dose and route of administration, warfarin dose, and INR values prior to and after vitamin K_1 administration were collected. Administration routes and doses of vitamin K_1 were assessed for compliance based on the ACCP guidelines.
RESULTS: Eighty-nine doses of vitamin K_1 were assessed and routes of administration included subcutaneous (39.3%), intravenous (37.1%), oral (13.5%), and intramuscular (10.1%). The most frequently prescribed dose was 10 mg (33.7%), followed by 2 mg (21.3%) and 5 mg (18%). Compliance rates (%) categorized by INR range were: < 5 (12%), 5-9 (28%), 9-20 (25%), and > 20 (17%). The overall compliance with ACCP-recommended doses and the routes of vitamin K_1 administration was only 18%.
CONCLUSION: The most frequently prescribed routes of administration for vitamin K_1 were subcutaneous and intravenous indicating the safer oral route is often not utilized. The prescribed doses of vitamin K_1 for the reversal of warfarin anticoagulation were highly variable and, in the majority of cases (82%), did not follow the recommended guidelines. The clinical significance of noncompliance with the ACCP guidelines for vitamin K_1 warrants further study.

118. Utilization of venous thromboembolism prophylaxis in acute medical illness. *Jason M. Enders, Pharm.D.*, Paul P. Dobesh, Pharm.D., BCPS, Joy R. Abu-Shanab, Pharm.D., BCPS, Jonathan E. Lakamp, Pharm.D., BCPS; St. Louis College of Pharmacy; St. Luke's Hospital; Sisters of Mercy Health System, St. Louis, MO.

PURPOSE: Hospitalized, medically ill patients are at risk for development of venous thromboembolism (VTE). The American College of Chest Physicians currently recommends unfractionated heparin (UFH) or low-molecular weight heparin (LMWH) for prevention of VTE in medically ill patients. Despite these recommendations, we hypothesized that the risk of VTE in this patient population is often underestimated and prophylaxis is underutilized. Our objective was to evaluate the utilization and appropriateness of prophylaxis in a medically ill population.
METHODS: A retrospective review of medically ill patients was conducted at our community hospital for patients with discharge dates between 1/2001 to 3/2002. Medically ill was defined as a non-ICU ≥ 6 day stay, and a primary diagnosis of CHF, pneumonia, or acute respiratory failure. Patient demographics, VTE risk factors, VTE prophylaxis utilization, development of symptomatic VTE, and hospital mortality were collected.
RESULTS: Data on 437 patients (63.8% male, mean age 77 ± 12 years, mean length of stay of 8.5 ± 5.1 days) were collected. Primary diagnoses included pneumonia (53.1%), CHF (39.1%) and acute respiratory failure (7.8%). The average number of risk factors was 2.53 ± 0.96. No prophylaxis was given to 49.4% of patients. According to published literature, appropriate prophylaxis was given in only 19.5% of patients. Symptomatic VTE occurred in 1.8% of patients. Overall, a 3% mortality rate was observed.
CONCLUSION: The rate of thromboprophylaxis utilization was lower than the rate identified by previous investigations and appropriate prophylaxis was infrequently utilized. Pharmacists should assume an increased role in improving adherence to VTE prevention guidelines.

119. Evaluation of enoxaparin usage for prevention of venous thromboembolism at a community-based teaching hospital. Eunice P. Chung, Pharm.D., *Judy S. Ling, Pharm.D.*, Jean M. Pallares, Pharm.D.; Western University of Health Sciences, Pomona, CA; Huntington Memorial Hospital, Pasadena, CA.

PURPOSE: This study evaluated the usage of low molecular weight heparin enoxaparin for prevention of venous thromboembolism (VTE) to 1) determine the cost-effectiveness of drug selection and dosage, and 2) evaluate the potential cost savings for the institution by implementing the VTE prophylaxis guideline approved by the Pharmacy, Therapeutics, and Dietary (PT & D) Committee.
METHODS: All orders of enoxaparin 30 mg or 40 mg during the month of February 2002 (N=150) were evaluated prospectively by reviewing the medical charts. VTE prophylaxis guideline pre-approved by the hospital PT & D Committee was used to evaluate the cost-effectiveness of drug selection and dosage. The hospital acquisition cost was used to determine the potential cost savings.
RESULTS: Of the evaluable orders (112/150), 72% were determined cost-ineffective usage of enoxaparin; 40% could have used less expensive unfractionated heparin and the remaining 60% could have used a lower dose of enoxaparin. Total hip replacement and total hip fracture was the most common indication (42%) for overall usage and was also the number one reason for cost-ineffective usage of enoxaparin (96%). Implementing the VTE prophylaxis guideline could have saved $4991.58 during the 4 weeks of study period, extrapolating to annual savings of $64,890.54 on drug acquisition cost.
CONCLUSION: Enoxaparin is an effective agent for VTE prophylaxis but only superior to unfractionated heparin for specific populations. The cost-effective dosage and frequency varies by indication. Significant cost savings can be achieved without compromising patient care, and implementing guidelines and standard orders may be effective methods.

120. TPA for central catheter clearance: does 1 mg = 2 mg? *Jodie M. Fink, Pharm.D.*, Kenneth M. Shermock, Pharm.D., Michael A. Militello, Pharm.D., BCPS, Donna Capozzi, Pharm.D., Thomas Hutson, D.O., Pharm.D., Matt Kalaycio, M.D., Brian Bolwell, M.D.; Cleveland Clinic Foundation, Cleveland, OH; Hospital of the University of Pennsylvania, Philadelphia, PA.

PURPOSE: The purpose of this study was to determine if tPA 1 mg/1 ml is as effective as 2 mg/2 ml for clearing central venous catheter occlusions.
METHODS: Adult patients with occluded Hickman catheters or implanted ports were randomized to receive tPA 1 mg or 2 mg. After tPA was instilled into the clotted lumen for 60 minutes, catheter function was assessed. A second dose was administered, if necessary. The primary end point was clearance rate after one dose. Clearance rates after two doses and adverse effects were also assessed. This equivalency trial required a total of 226 lumens to show that the 1 mg dose was not more than 10% worse than the 2 mg dose.
RESULTS: A total of 61 lumens (67% Hickmans, 33% ports) were enrolled. Enrollment was stopped early due to lower than expected subject accrual. TPA 1 mg was administered to 37 (61%) of the lumens. The first dose clearance rates were 81.1% for tPA 1 mg and 83.3% for tPA 2 mg (% difference = -2.3% [95% CI: -18.7 to 14.1] (NS). Clearance rates after one or two doses were 86.5% for tPA 1 mg and 87.5% for tPA 2 mg (% difference -1.0% [95% CI: -15.5 to 13.4] (NS). No bleeding events were observed.
CONCLUSION: Although the clearance rates tPA 1 mg and tPA 2 mg were similar, statistical significance was not achieved due to the small sample size. Therefore, the relative effectiveness of tPA 1 mg verses tPA 2 mg for central catheter clearance remains undetermined.

121. Impact of low molecular weight heparins on acute venous thromboembolism prophylaxis: a case-control analysis. *Shellee A. Grim, Pharm.D.*, Kenneth E. Record, Pharm.D., BCPS, Daniel A. Lewis, Pharm.D., Kelly M. Smith, Pharm.D.; University of Kentucky, Lexington, KY.

PURPOSE: An increased incidence of venous thromboembolism (VTE) was suspected among trauma and orthopedic patients receiving a low-molecular weight heparin (LMWH) at our institution during a two-month period. The objectives of this study were to determine the frequency of VTE and identify risk factors associated with VTE development in this patient population.
METHODS: A retrospective chart review of university hospital patients during a six-month period was conducted. Patients were included if they were admitted to the trauma or orthopedic surgery services and received either dalteparin or enoxaparin for prevention of VTE. The case group was defined as patients developing clinically overt VTE following LMWH administration. The control group, defined as patients meeting inclusion criteria that did not develop VTE, was selected in a 2:1 ratio to the cases.
RESULTS: A total of 161 patients received dalteparin and 49 received enoxaparin. Eleven (6.8%) dalteparin patients developed VTE, compared to 6 (12%) enoxaparin patients. Forty-one percent of the cases failed to receive LMWH within 48 hours of admission, compared to 14% of controls. A greater percentage of patients at high risk of developing VTE, from either single or cumulative risk factors, was found in cases (76% vs. 38-57% of controls).
CONCLUSION: We demonstrated a low incidence of VTE in trauma and orthopedic patients receiving LMWH for VTE prophylaxis. Data suggests that the perceived increased incidence of VTE may be attributed to LMWH timing and a large percentage of patients at high risk of developing a VTE.

122. Consistency of fondaparinux superiority for venous thromboembolism prevention in orthopedic surgery according to different composite efficacy end points. *David W. Hawkins, Pharm.D.*, Kenneth A. Bauer, M.D., Bengt I. Eriksson, M.D., Michael R. Lassen, M.D., Alexander G.G. Turpie, M.D.; Mercer University, Atlanta, GA; Beth Israel Deaconess Medical Center, Boston, MA; Sahlgrenska University Hospital, Goteborg, Sweden; Hilleroed Hospital, Copenhagen, Denmark; Hamilton General Hospital, Hamilton, Canada.

PURPOSE: In a fondaparinux phase III program in major orthopedic surgery, fondaparinux demonstrated superior efficacy over enoxaparin (overall risk reduction 55.2%, $p<0.001$) without increasing clinically relevant bleeding. The objective of this study was to compare the efficacy of fondaparinux versus enoxaparin for venous thromboembolism (VTE) prevention, according to different composite end points, in this setting.
METHODS: In 4 multinational, randomized, double-blind, phase III trialsæ1 in hip-fracture, 2 in hip replacement, and 1 in knee replacementæthe predefined composite primary efficacy end point was VTE incidence up to day 11 defined as mandatory bilateral venography detection, or documented symptomatic deep-vein thrombosis (DVT) or pulmonary embolism (PE). To match the composite efficacy end points recently suggested for superiority

studies by the American College of Chest Physicians (ACCP) Consensus (any proximal DVT + fatal PE + symptomatic proven DVT or PE) and the Committee for Proprietary Medicinal Products (CPMP, any proximal DVT + symptomatic proven PE + death from any causes including fatal PE), post-hoc analyses were performed.
RESULTS: According to criteria predefined in the protocol, the efficacy endpoint incidences up to day 11 were 6.8% (182/2682) and 13.7% (371/2703) for fondaparinux versus enoxaparin, respectively (-55.2% OR [-63.1%, -45.8% CI], p=0.0001). The efficacy endpoint incidences according to ACCP criteria were 1.7% (47/2764) and 3.3% (92/2780) for fondaparinux versus enoxaparin, respectively (-49.6% OR [-65.5%, -27.3%], p=0.0001); and 2.1% (57/2775) and 3.9% (108/2797), respectively (-48.0% OR [-63.2, -27.3], p=0.0001), according to CPMP criteria.
CONCLUSION: The superior efficacy of fondaparinux over enoxaparin for VTE prevention in major orthopedic surgery was consistent and maintained whatever composite endpoints considered.

123. A comparison of the accuracy of the Coaguchek S® and the Coaguchek® point of care devices with a standard laboratory instrument. *Vincent J. Colucci, Pharm.D., BCPS*, C. Eugene Mead, Ph.D., Joyce Hickethier, R.N., Lisa Dean, R.N., Demarise Raunig, R.N.; University of Montana, Missoula, MT.

PURPOSE: This study compared the accuracy of international normalized ratio (INR) results from point of care (POC) testing devices to that of a standard laboratory instrument and with each other to establish and confirm reliable INR results for anticoagulation evaluation.
METHODS: Routine INRs of 42 chronically anticoagulated patients were measured with the Coaguchek S® (Roche Diagnostics) POC device using fingerstick capillary whole blood and compared to a standard laboratory instrument (Sysmex® CA-500: Dade Behring, Deerfield, Il) and the older Coaguchek® POC device using venous blood samples acquired via venipuncture. Linear regression methods were used to analyze the extent, significance, and variation of the relationship between the instruments. Paired sampling (t-tests) were used to measure and compare INR differences between instruments.
RESULTS: The Coaguchek S correlated positively with the lab instrument measurement (r=0.97) by orthogonal regression analysis. Similarly, the Coaguchek demonstrated a favorable correlation (r=0.94) with the laboratory instrument. Additionally, the POC devices correlated positively with each other (r=0.98). These associations decreased with INR values > 4. Paired sampling revealed mean INR differences of 0.079 ± SD 0.666, p=0.44 (Coaguchek S vs. Lab Instrument) and 0.196 ± SD 0.712, p=0.09 (Coaguchek vs. Lab Instrument).
CONCLUSIONS: POC testing devices (Coaguchek S and Coaguchek) compare favorably in accuracy with a standard laboratory instrument and with each other with INR values <4 suggesting no clinical difference in therapeutic planning of anticoagulation regimens. Repeating or cross-checking INR values above 4 with POC device with the lab instrument may be warranted.

124. Optimal international normalized ratio in Thai patients with mitral valve replacement. *Siriporn Krittathanmakul, M.Pharm.*, Wibul Wongpoowarak, M.Sc.; Prince of Songkla University, Songkla, Thailand.

PURPOSE: To determine the optimal range of international normalized ratio (INR) in warfarinized patients with mitral valve replacement (MVR) at the teaching hospital in Southern Thailand.
METHODS: Patients with MVR who received oral anticoagulant and had stable INRs were eligible. The following information was collected by retrospective chart reviews: sex, age, date of valve replacement, all INR values, complications including bleedings and thromboembolism, and hospital admissions. Optimal INR was defined as the INR values that did not cause either bleedings or thromboembolism.
RESULTS: The data were collected on 69 patients, 29 males and 40 females. Mean age of patients and mean duration of follow up were 41 years and 6.61 years, respectively. With 1942 INR values, the optimal range of INR was between 1.7-2.95. The incidence of minor bleedings were 13.17% patient-years, most common sites were gum, skin, and vagina. Thromboembolism was reported 7.02% patient-years, most common sites were brain, chest, and limbs. There were 12 hospital admissions, 8 events due to thromboembolism and 2 events due to bleedings.
CONCLUSIONS: The optimal intensity of anticoagulant therapy for Thai patients with MVR, that could effectively prevent thromboembolism and avoid bleedings, was between 1.7-2.95. This range was lower than the range recommended by the American College of Chest Physicians (2.5-3.5). Factors that may be responsible for this finding should be further evaluated.

Herbal Medicine

125. The use of complementary and alternative medicines by patients taking digoxin. *Stephen Shalansky, Pharm.D.*, Erin Neall, B.Sc.Pharm.; St. Paul's Hospital; University of British Columbia, Vancouver, BC, Canada.

PURPOSE: While there are many potential interactions between digoxin and complementary and alternative medicines (CAMs), the usage patterns amongst digoxin patients are unknown. The purpose of this study was to determine the prevalence of CAM use, and types of CAMs used, amongst a cohort of patients taking digoxin. Exposures to other medications reported to interact with digoxin were also recorded.
METHODS: Patients taking digoxin were identified through review of cardiac rehabilitation clinic, and atrial fibrillation clinic records. Those consenting to participate were given a structured survey including questions regarding use during the prior month of specific CAMs and over-the-counter (OTC) medications reported to interact with digoxin. Patients were also asked about recent symptoms associated with heart failure or atrial fibrillation, and symptoms of digoxin toxicity. Prescription medication use was identified through review of the provincial prescription claims database.
RESULTS: Vitamins and supplements had been used by 34 of 57 (60%) surveyed patients in the 30 days prior to the survey, while herbal products had been used by 10 patients (18%). The most common vitamins consumed were B vitamins (42%), vitamin E (32%), multivitamins (23%), and vitamin C (21%). The most common supplement was coenzyme Q_{10} (7.0%), while saw palmetto (4%) was the only herbal product was used by more than one patient. Only 2 patients (4%) used CAMs reported to interact with digoxin (one patient used cascara and C. angustifolia, one patient used ginseng). In contrast, 28% used a potentially interacting OTC medication (excluding potassium) and 83% used a potentially interacting prescription medication. There was no statistically significant association between reported signs of disease state exacerbation (CHF or atrial fibrillation) or digoxin toxicity, and the exposures queried.
CONCLUSIONS: While overall use of CAM was common amongst this cohort of digoxin patients, exposure to potentially interacting CAMs was relatively rare.

126. The impact of complementary and alternative medicine use on warfarin-related adverse outcomes. *Stephen Shalansky, Pharm.D.*, Erin Neall, B.Sc.Pharm., Melissa Lo, Esther Abd-Elmessih, B.Sc., Linda Vickars, M.D., Larry Lynd, BSP, Ph.D. candidate; St. Paul's Hospital; University of British Columbia, Vancouver, BC, Canada.

PURPOSE: To identify the prevalence of complementary and alternative medicine (CAM) use, and the associated adverse outcomes, amongst a cohort of patients taking warfarin.
METHODS: Patients taking warfarin were identified through review of pharmacy, cardiac rehabilitation clinic, anticoagulation clinic, and atrial fibrillation clinic records. Those consenting to participate were given a structured survey including questions regarding the use over the past month of specific CAMs and over-the-counter (OTC) medications reported to interact with warfarin. Patients were also asked about bleeding events. Prescription medication use was identified through review of the provincial prescription claims database, and INR values were obtained from laboratory records.
RESULTS: The survey was completed by 156 patients, 72 (46%) of whom reported use CAM use over the past month including 57 (37%) who had used CAM reported to potentially interact with warfarin. The most common potentially interacting CAMs were vitamin E (28%), garlic (10%), and chamomile (6%). Sixty-eight patients (44%) reported bleeding events over the past month. Of the 139 patients for whom INR results were available, 15 (11%) had INRs ≥ 4 during the past month. Comparing patients who did and did not report the use of CAMs that could potentially increase the risk of bleeding or elevated INR, there was neither a significant difference in the incidence of bleeding (37% versus 47% respectively, p=0.21) nor the incidence of INR results ≥ 4 (4% versus 14% respectively, p=0.10).
CONCLUSION: While use of potentially interacting CAM was common amongst this cohort of warfarin patients, it did not appear to increase the risk of bleeding or having an elevated INR.

127. Predicting the intention to use herbal medicines using the Theory of Planned Behavior in older Veterans Affairs outpatients. *Aditya A. Marfatia, B.S.*, Gireesh V. Gupchup, Ph.D., Dennis W. Raisch, Ph.D., Marcia M. Worley, Ph.D., Mary Bartley, Pharm.D., Brenda Bennett, Pharm.D.; University of New Mexico; Veterans Affairs Cooperative Studies Program; Clinical Research Pharmacy Coordinating Center, Albuquerque, NM.

PURPOSE: The purpose of this study was to identify the predictors of the intention to use herbal medicines within the next six months among older Veterans Affairs (VA) outpatients, using the Theory of Planned Behavior (TPB).
METHODS: A questionnaire was administered to a convenience sample of 206 outpatients at the VA hospital in Albuquerque, NM. Patients were included in the sample if they were 65 years of age or older, community dwelling, English speaking, did not have a known diagnosis of dementia, and were either Hispanic or non-Hispanic white. Hierarchical regression analysis was performed to identify significant predictors of intention to use herbal medicines within the next six months.
RESULTS: A useable response rate of 73.3 percent (n=151) was obtained. Hierarchical regression analysis indicated that the only significant predictor of the intention to use herbal medicines within the next six months was the respondents' attitude towards taking herbal medicines ($\beta = 0.69$, $p<0.001$).

The other variables in the TPB, subjective norms, or what others think about taking herbal medicines, and perceived behavioral control, were not significant predictors of intention to use herbal medicines within the next six months. The Adjusted R^2 for the hierarchical regression model was 0.58, $p<0.001$.
CONCLUSION: Attitude towards taking herbal medicines is a strong predictor of the intention to use herbal medicines within the next six months among older VA outpatients. These findings have important implications for pharmacy practitioners as they develop counseling strategies about herbal medicines for older VA outpatients.

128. Comparison of recommendations made by pharmacists and health food store employees in a depressed patient. James K. Glisson, M.D., Pharm.D., *Holly E. Rogers, Pharm.D.*, Sara L. Noble, Pharm.D.; University of Mississippi Medical Center; Pfizer, Inc., Jackson, MS.

PURPOSE: Literature regarding health food store employees' and pharmacists' recommendations for alternative therapies is scarce. This study was conducted to evaluate the advice pharmacists and health food store employees provide to customers concerning the use of dietary supplements in a given case scenario dealing with anxiety and depression.
METHODS: The survey was performed as a simulated consumer case encounter in 32 health food stores and 38 retail pharmacies. Prior to conducting the survey, the case scenario was reviewed and approved by 4 board certified primary care physicians. All customer questions were asked in a specific order to maintain consistency, and each investigator made notes during the interaction, providing additional information only if elicited, such as the use of Ma huang.
RESULTS: Past medical history, concurrent medications, and allergies were not consistently determined prior to the given advice. Eighty-eight percent of health food stores employees and 60% of pharmacists suggested the use of at least one product; however, less than 20% in each group asked about concurrent medications. Twelve pharmacists, 32%, recommended seeing a physician for evaluation; however, no person asked about existing medical conditions. Only 1 health food store employee asked if any allergies existed, and eight stated that it was appropriate to use the recommended product during pregnancy. No pharmacists made this recommendation. Finally, approximately 75% of those surveyed stated the recommended products were devoid of side effects.
CONCLUSION: The quality of information provided to consumers as they consider the use and purchase of dietary supplements is of major concern. This study identifies several areas that need addressing.

129. Use of dietary supplements in a rural Mississippi clinic population. J. Emmy Steevens, Pharm.D., James K. Glisson, M.D., Pharm.D., *Holly E. Rogers, Pharm.D.*, Emily C. Dix, Ph.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: Demographics of dietary supplement users in metropolitan areas are well documented. Limited data exists on usage patterns in rural America. The purpose of this investigation was to determine patients' patterns, reasons for use, opinions regarding safety, regulation and efficacy, and patients' perceptions of health care provider knowledge of dietary supplements.
METHODS: The survey was conducted in a rural, Mississippi family medicine clinic. Patients provided information such as frequency, number and approximate monthly expenditure of supplements, and how likely they would be to take recommendations by a physician, pharmacist, health food store employee, or friend. Patients were asked to rate their perception of the dietary supplement knowledge of pharmacists, physicians, and health food store employees.
RESULTS: One hundred fifty-one patients completed the survey. The majority of dietary supplement users were white (88.2%) and female (71.6%). The most common reasons for use were general health (68.6%), energy (28.4%) and weight loss (19.6%). The most common sources for information on dietary supplements were physicians (35.3%), friends (25.5%), relatives (23.5%), and magazines (22.5%). When asked to identify the best source of information, physicians (31%) were cited most frequently, followed by pharmacists (9%), and herbalists (8%). Both users and nonusers agreed dietary supplements undergo the same federal government approval process as pharmaceutical drugs, requiring them to be proven safe before sold in stores.
CONCLUSION: This study demonstrates patient misperception of quality and regulatory issues concerning supplements. It describes patient willingness to discuss and implement recommendations for supplement use with non-healthcare providers despite believing physicians and pharmacists are knowledgeable.

130. The clinic at the health food store: employee recommendations for depression and product analysis by HPLC. *Holly E. Rogers, Pharm.D.*, James K. Glisson, M.D., Pharm.D., Ehab A. Abourashed, Ph.D., Richard L. Ogletree, Pharm.D., Charles D. Hufford, Ph.D., Ikhlas Khan, Ph.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: Increasing numbers of patients are self-medicating with dietary supplements. Significant concern exists among healthcare providers regarding the composition, safety, and efficacy of these supplements. Furthermore, patients may receive medical advice within health food stores. The purpose of this study was determine specific products health food store employees recommend for depression and to compare the actual content of these products determined by HPLC to the stated label content.
METHODS: Twelve health food stores were selected for inclusion. A single investigator conducted all inquests by approaching one employee within each store and asking, "What do you recommend for depression?" Five additional questioned were then posed to elicit further information. Products containing St. John's Wort were purchased and analyzed for hypericin and pseudo-hypericin content via HPLC and then used to calculate total hypericins content.
RESULTS: Numerous comments made by health food store employees regarding St. John's Wort and the treatment of depression were inaccurate and potentially unsafe. No product contained ± 10% of the stated label claim for hypericin, and two products contained 0% hypericin. However, two products' total hypericins content was within ± 10% of the label claim for hypericin alone.
CONCLUSIONS: Health food store employees offer healthcare advice regarding the treatment of depression with dietary supplements. Furthermore, the discrepancies noted between actual product content and manufacturers' label claims continue to raise concern for those patients who choose to employ these agents as medical treatment. These inconsistencies will continue to be a significant barrier to acceptance by the conventional medical community until reliable, good quality products are available.

131. Complementary and alternative medicine: Tennessee pharmacists' usage, counseling and referral practices. *Peter A. Chyka, Pharm.D.*, Glen E. Farr, Pharm.D.; University of Tennessee Health Science Center, Memphis, TN.

PURPOSE: To determine the extent and variety of Tennessee pharmacists' use of complementary and alternative medicine (CAM) therapies and providing advice or referral thereon.
METHODS: During Autumn 2001 a 60-item survey was administered to pharmacists who participated in one of five continuing education programs conducted throughout Tennessee. Inclusion criteria included completion of all survey elements and a Pharmacy practice in Tennessee.
RESULTS: A total of 650 surveys were submitted and 349 met the inclusion criteria. Of these, 317 pharmacists (90.8%) personally used (n=299, 85.6%), advised patients (n=258, 73.9%) or referred individuals (n=267, 76.5%) for CAM, termed "CAM-practice." The top two approaches for which pharmacists were unsure of the definition were body work (48.4%) and biofeedback (32.4%), that they personally used were dietary supplements (61.0%) and spiritual healing (54.7%), for which they referred patients were dietary supplements (55.0%) and chiropractic (38.7%), and on which they counseled patients were dietary supplements (66.5%) and spiritual healing (33.8%). The use of CAM was more likely (OR=2.8, CI 1.5, 5.2) by a pharmacist in a community pharmacy practice (90.5%) compared those in other practices (77.3%). The number of years in practice and geographic region did not affect the frequency of CAM-practice. An adverse event from CAM in the past year was suspected more often by pharmacists who did not CAM-practice (75.0%) than those who did so (29.3%, $p<0.001$). Further education on CAM was desired by 79.4% of respondents.
CONCLUSION: Most Tennessee pharmacists use CAM therapies and provide advice or referral thereon; they desire additional education on CAM.

132. Prospective randomized evaluation of herbal product use in surgical patients. *José O. Rivera, Pharm.D.*, Mona Liza R. Valentin, Pharm.D., Emmett L. McGuire, M.D., Kallol Chaudhuri, M.D.; University of Texas; Texas Tech University Health Science Center, El Paso, TX.

PURPOSE: To evaluate the use of herbal supplements among surgical patients in a predominantly Hispanic population.
METHODS: Prospective randomized evaluation of patients aged 18 years or older scheduled for surgery. Prior to surgery, a 15 to 30 minute semi-structured interview was conducted focusing on the use of herbal products that have associated with adverse events. Two days after surgery, the interviewer conducted a chart review recording any complications that the patient experienced during or after surgery.
RESULTS: Seventy percent of our sample (N=115) admitted to using herbal products. About 58% of patients rated the products as "excellent" in treating their conditions and 92% of them did not inform their physician of their use. Among the herbal products that were used, 18% of the products are known to cause adverse reactions, 12% are associated with causing drug interactions, and 10% are known to negatively interact with specific disease states. Nine patients who reported using herbs had complications during and two days post surgery.
CONCLUSION: With the growing use of herbal products and because most user do not inform their physician, there is increasing concern related possible herbal related adverse events during surgery. The current study documented at least 141 instances that may lead to herbal related adverse events. Eleven percent of herbal users had documented complications during surgery. A thorough examination of a patient's medication history including use of herbal products should consistently be performed in order to minimize complications during and after surgery.

133. Use of herbal products in asthmatic living on the U.S./Mexican border. *José O. Rivera, Pharm.D.,* Harold W. Hughes, M.D., Sean M. Connery, M.S.; University of Texas; Texas Tech University, El Paso, TX.

PURPOSE: To evaluate the prevalence of herbal products (HP) usage in adult, asthmatics requiring hospitalization.
METHODS: A retrospective chart review of admissions for asthma was conducted to determine HP documentation. Subsequently, a prospective, semi-structured interview analysis was conducted in patients who were admitted for asthma exacerbations for a one-year period. A bilingual interviewer was used to evaluate types and frequency of HP used specifically for the treatment of asthma.
RESULTS: A total of 67 cases were reviewed retrospectively while 60 were interviewed. We found no documentation of HP use by chart review while prospective interviews showed 41.7% using HP. Of the 25 who used HP the most common were: oregano 28%, chamomile 20%, garlic 16%, eucalyptus 12%, and lemon 12%. A total of 8 patients reported taking an HP that could possibly result in a drug interaction with an anti-asthmatic medication or could actually exacerbate the asthma. In addition, another 16 patients reported using an HP that could interact with other drugs or cause other types of adverse reactions. Of greatest concern is the use of these herbs as essential oils either taken internally or applied directly to nasal passages.
CONCLUSION: There is an obvious lack of documentation regarding herbal product use in medical records most likely due to the fact that many healthcare providers may not be aware of the effects of herbal products. Some herbal products used in our population could actually interact with anti-asthmatic agents and/or result in compromised asthma control, therefore this information should be included in routine history examinations.

HIV/AIDS

134. Nelfinavir-induced glucose intolerance in pregnancy: placental and fetal outcomes in rats. *Patty Fan-Havard, Pharm.D.,* Cheryl A. Lieb, Pharm.D., Eunsun Cho, Pharm.D., Sarah K. Wymer, Pharm.D., Cliff M. Monahan, D.V.M., Ph.D.; Ohio State University, Columbus, OH.

PURPOSE: HIV-1 PIs are associated with glucose intolerance. Gestational diabetes (GD) is associated with maternal-fetal complications. We investigated the placental (PL) and fetal outcomes following in utero exposure to NFV in rats.
METHODS: A total of 21 female Sprague-Dawley rats were randomly assigned to a control (C), low dose (LD) NFV (100 mg/kg/day) or high dose (HD) NFV-treated (400 mg/kg/day) group. Rats were mated overnight. Sperm-positive vaginal smears denoted day 0 of pregnancy. Necropsy was performed at day 20 of gestation. The placentas and fetuses were isolated, weighed and measured. Fetal livers (FL) were removed and weighed. Maternal plasma glucose (MPG) was determined. Two pathologists performed histology reviews in a blinded-manner. Data were analyzed by ANOVA, Tukey post hoc testing, and with significance at $p<0.05$.
RESULTS: Necropsy was performed on 7 C (total of 100 concepti), 8 LD (118 concepti) and 6 HD NFV-treated (77 concepti) dams. The mean (± SEM) PL weight ratios were 0.49 ± 0.005 gms, 0.53 ± 0.005 gms and 0.52 ± 0.008 gms in C, LD and HD NFV-treated groups, respectively ($p<0.001$). The PL surface area (SA) was significantly larger in the LD and HD NFV-treated groups as compared to C ($p<0.05$). A significantly lower FL weight ratio was observed in the LD and HD NFV-treated groups as compared to C ($p<0.001$). NFV-treated dams had higher glucose levels, but the difference was not statistically significant. Diffuse congestion, multifocal telangiectasia, and myeloid and erythroid hyperplasia were observed for all FL in both LD and HD NFV-treated dams.
CONCLUSIONS: Our data suggest the alterations in PL weight and SA and FL weight ratios are consistent with experimental model of GD, despite a lack of statistical difference in MPG.

135. Effect of ritonavir-containing regimens on lipids compared to other protease inhibitors. Susan Haselkorn, Pharm.D., *Marisel Segarra-Newnham, Pharm.D., BCPS;* Veterans Affairs Medical Center, West Palm Beach, FL.

BACKGROUND: Protease inhibitor (PI) therapy may cause increases in lipids. Ritonavir appears to cause the largest increase in a dose-dependant fashion. However, there are limited data on how different protease inhibitors compare with each other within the same patient.
PURPOSE: To evaluate the effect of ritonavir-containing regimens on triglycerides (TG) and total cholesterol (TC) compared to other PIs on patients followed at an HIV clinic.
METHODS: Patients on ritonavir-containing PI regimens after treatment failure with other PI's were evaluated. All patients who had lipid values available while on other PI and after ritonavir were included. The following data were collected: age, body mass index, anti-retroviral regimen, TC and TG during non-ritonavir PI therapy and after ritonavir therapy. The addition or change in lipid-lowering therapy was also recorded. Eleven patients were needed for 90% power to detect a 50-point change in TC or TG. The institutional review board approved the study.
RESULTS: Eighteen patients were eligible for inclusion. Fifty-six percent of patients were receiving ritonavir 100 mg BID and 38% were receiving ritonavir 400 mg BID. A significant increase in both TC and TG was seen in patients receiving ritonavir-containing regimens compared to other PIs (TC 229 vs. 204 and TG 313 vs. 213, $p<0.05$, paired t-test). Three patients were receiving lipid-lowering therapy prior to ritonavir with one needing a dose adjustment after the addition of ritonavir. Two patients were started on lipid-lowering therapy and one on low fat diet after ritonavir was initiated. The clinical pharmacist is following all these patients.
CONCLUSIONS: Patients who are to start ritonavir therapy need to be closely monitored for changes in TC and TG. Changes or addition of lipid-lowering therapy may be needed even if other PI did not cause a change in lipid values. A clinical pharmacist can provide the follow up necessary and adjust medications as indicated.

136. Characteristics of metabolic abnormalities and lipodystrophy associated with drug therapy in human immunodeficiency virus-infected children. *Sandra Benavides, Pharm.D.,* Katalin Koranyi, M.D., Milap C. Nahata, Pharm.D.; Ohio State University; The Children's Hospital, Columbus, OH.

OBJECTIVES: The objective of the study was to assess the characteristics of metabolic abnormalities and lipodystrophy in HIV infected children and determine their association with antiretroviral medications.
METHODS: Medical records of all pediatric patients seen at the Immunodeficiency Clinic at Children's Hospital, Columbus, Ohio from July 1, 1999 to July 31, 2001 were reviewed. The data on patient demographics, date of diagnosis, antiretroviral medication history, laboratory results, and evidence of lipodystrophy were collected. Endpoints included evidence of lipodystrophy, elevated serum glucose, cholesterol and/or triglyceride concentrations. Descriptive statistics were compiled and patients were stratified into two groups (evidence of abnormality or not) for each endpoint. Cross tabulations were used to determine if antiretroviral history differed between groups.
RESULTS: Twenty-two pediatric patients (M=13, F=9), ages 1.6-16.4 years, were included in the study. Of these patients, two (9.1%) developed lipodystrophy, 13 (51%) hypercholesterolemia, 13 (51%) hypertriglyceridemia, and one hyperglycemia. Mean serum cholesterol concentrations was 206 mg/dL (SD ± 37) and mean serum triglyceride concentration was 232 mg/dL (SD ± 154). These values were statistically higher than normal values for pediatric patients. The history of indinavir utilization was approaching significance ($p=0.06$) for those patients developing lipodystrophy. Increased serum glucose, cholesterol and triglyceride concentrations did not correlate with any specific agent or length of treatment with any specific drug. The correlation among the disorders was not significant.
CONCLUSIONS: Pediatric patients infected with HIV developed elevations in cholesterol and triglycerides. As also seen in the adult HIV literature, the specific agents or cause of these abnormalities is not clearly defined.

137E. Abacavir systemic clearance in children is highly influenced by glucuronidation phenotype. *John H. Rodman, Pharm.D.,* Shane J. Cross, Pharm.D., Lawrence J. D'Angelo, M.D., M.P.H., C. Rose, Brian L. Robbins, Ph.D., Geoffrey K. Yuen, Pharm.D.; St. Jude Children's Research Hospital, Memphis, TN; Children's National Medical Center, Washington D.C.; GlaxoSmithKline, Research Triangle Park, NC.

Presented at the 14th Annual International AIDS Conference, Barcelona, Italy, July 7-12, 2002.

Infectious Diseases

138. Impact of clinical pharmacists on vaccination rates in medicine, surgery, and infectious disease services: a randomized, controlled trial. *Peter Dumo, Pharm.D.,* John Dougherty, Pharm.D., Monica Shieh, Pharm.D.; Wayne State University; Harper University Hospital, Detroit, MI.

PURPOSE: We evaluated the impact of clinical pharmacist (CP) on inpatient pneumococcal (PV) and influenza vaccination rates (IV) in 3 patient care services: surgery patients, medicine and infectious diseases(ID).
METHODS: Patients admitted to Harper University Hospital from 11/01 to 3/2 and who were being followed by a CP on the medicine, surgery or ID service were enrolled. Patients were randomized (by admission date) to active CP involvement for vaccination or usual care. Screening and recommendations were incorporated into the CP's daily schedule.
RESULTS: IV and PV rates increased in all groups ($p<0.05$) except for IV in the surgery group.

	Medicine R.Ph./M.D.	ID R.Ph./M.D.	Surgery R.Ph./M.D.
N	124/126	137/103	21/25
Age	66.7/68.9	49.7/52.3	59.7/65.4
Comorbidities	3/3	1/1	1/2
Previously Vaccinated			
Influenza	61 (49.2%)/49(38.9%)	58 (42.3%)/27(25.2%)	12 (57%)/9(36%)
Pneumococcal	38 (30.6%)/41(32.5%)	71 (51.8%)/27(25.2%)	7 (33%)/6(24%)

Eligible for hospital vaccination			
Influenza	63/77	78/56	10/15
Pneumococcal	86/85	57/54	12/19
Received vaccine in-hospital			
Influenza (%)	51 (81.0%)*/5(4.0%)	69 (88.5%)*/1(1.8%)	5 (50%)/2(13%)
Pneumococcal(%)	73 (84.9%)*/5(4.0%)	49 (86%)*/2(3.7%)	4 (33%)*/0(0%)

*p<0.01 compared to M.D. group

CP recommendations increased the IV rate from 5% to 83% and the PV rate from 5% to 82% (p<0.01 for both). The CP caring for surgical patients evaluated fewer patients and was less successful at increasing vaccination (p<0.05). Predictors of previous vaccination included month of admission and being immunocompromised(p<0.05).
CONCLUSION: CP can dramatically increase IV and PV rates in hospitalized patients. Reasons for low screening and vaccination rates in surgical patients need to be investigated.

139. Impact of new and proposed MIC breakpoint changes on the in vitro activity of penicillin and ceftriaxone against non-meningeal isolates of *Streptococcus pneumoniae*. *Michael B. Kays, Pharm.D.,* Gerald A. Denys, Ph.D., Daryl J. Hoban, Ph.D.; Purdue University, Indianapolis, IN; Clarian Health Partners, Inc., Methodist Hospital, Indianapolis, IN; International Health Management Associates, Inc., Schaumburg, IL.

The clinical significance of β-lactam resistance in non-meningeal (NM) isolates of *Streptococcus pneumoniae* (SP) is debatable. Penicillin (PEN) and ceftriaxone (CTRX) MIC breakpoints (BP) were originally based on achievable CSF concentrations. In 2000, the Drug-Resistant SP Therapeutic Working Group (DRSPTWG) recommended separate PEN BP for patients with pneumococcal pneumonia. In 2002, the NCCLS increased CTRX BP for NM isolates of SP.
PURPOSE: To evaluate the impact of MIC BP changes on the in vitro activity of PEN and CTRX against NM isolates of SP.
METHODS: Clinical, non-duplicate SP isolates (n=4,735) cultured from NM (respiratory, blood) sources from 1999 to 2000 were studied. PEN and CTRX MICs were determined by E-test according to manufacturer's guidelines. PEN MICs were interpreted using the NCCLS BP (susceptible [S], ≤ 0.06 µg/ml; intermediate [I], 0.12-1 µg/ml; resistant [R], ≥ 2 µg/ml) and the proposed DRSPTWG BP (S, ≤ 1 µg/ml; I, 2 µg/ml; R, ≥ 4 µg/ml). CTRX MICs were interpreted using the previous NCCLS BP (S, ≤ 0.5 µg/ml; I, 1 µg/ml; R, ≥ 2 µg/ml; M100-S11, 2001) and the new NCCLS BP (S, ≤ 1 µg/ml; I, 2 µg/ml; R, ≥ 4 µg/ml; M100-S12, 2002).
RESULTS: The MIC_{50} and MIC_{90} were 0.047 µg/ml and 2 µg/ml for PEN and 0.03 µg/ml and 1 µg/ml for CTRX, respectively. For PEN, S, I, and R were 59.0%, 20.4%, and 20.6% using the NCCLS BP and 79.4%, 11.3%, and 9.3% using the proposed DRSPTWG BP. For CTRX, S, I, and R were 81.2%, 13.7%, and 5.1% using the previous NCCLS BP and 94.9%, 3.7%, and 1.4% using the new NCCLS BP. CTRX-R decreased from 1.9% to 0.6% for PEN-I and from 22.9% to 6.0% for PEN-R strains using the new NCCLS BP.
CONCLUSIONS: The percentage of NM SP isolates reported as I and R to PEN and CTRX is markedly decreased when MICs are interpreted using the new or proposed BP. However, continued surveillance of resistance trends is necessary as isolates may remain resistant to these agents despite BP changes.

140. Pharmacodynamics of antifungal agents in human candida infections. *John D. Cleary, Pharm.D.,* Donna Sullivan, Ph.D., Stanley. W. Chapman, M.D.; University of Mississippi, Jackson, MS.

BACKGROUND: Some toxicity and activity of anti-mycotics can be predictable based on changes in gene expression profiles. However, mycotic organisms alter the host cell milieu in attempts to improve pathogen survival. We evaluated the affects of fungal infections on anti-mycotic induced human gene expression in vivo.
METHODS: Patients with disseminated candidiasis treated with an azole, polyene or echinocandin were evaluated. Total RNA was isolated from cells obtained during peripheral venepuncture using the Triazole reagent. cDNA was synthesized using anchoring primers and labeled using Cy3 or Cy5. Complimentary DNA were then hybridized to a human gene array containing >12,000 known genes. The identity of specific genes with altered regulation (> 2 fold) was performed by using variable intensity analysis between the two exposures. Significant genes are validated using RT-PCR with unique primers.
RESULTS: Three hundred twenty-one up and 551 down-regulated cDNAs were considered unique to one of the treatment groups. Transcriptional regulatory pathways were accentuated by therapy. In addition, cellular defenses appeared enhanced based on significant increases in hematopoietic stem/progenitor cells protein, colony stimulating factor 3 receptor (granulocyte), interleukin 16 (lymphocyte chemoattractant factor), mitogen-activating protein kinase 1 through 4, vascular cell adhesion molecule 1, vacuolar protein sorting protein 11, vacuolar proton pump Δ polypeptide, secretogranin II, α 1 integrin, T cell receptor Δ locus, and T cell receptor Δ.
CONCLUSIONS: These studies have identified a number of genes with altered regulation associated with anti-mycotic therapy. Further investigation may still elucidate novel pathways involved in anti-mycotic activity.

141. Impact of desoxycholate on amphotericin B-induced differential gene expression. *John D. Cleary, Pharm.D.,* Stanley. W. Chapman, M.D.; University of Mississippi, Jackson, MS.

BACKGROUND: Toxicity and activity of amphotericin B may be predictable based on changes in gene expression. However, the solubilizing agent, desoxycholate (DOC) has been associated with significant toxicity. We evaluated the affects of DOC on human monocyte (THP-1) gene expression in vitro to amphotericin B.
METHODS: THP-1 cells (5.0 x 10^6 cells) were exposed in triplicate for 2-6 hours to DOC 20.2 ug/mL, amphotericin B 5 ug/mL solubilized with DOC or media. Cell viability was equivalent in each group. Total RNA was isolated from cells using the Triazole reagent. cDNA was synthesized using anchoring primers and labeled using Cy3 or Cy5. Complimentary DNA were then hybridized to a human gene array containing >12,000 known genes. The identity of specific genes with altered regulation (> 2 fold) was performed by using variable intensity analysis between the two exposures. Significantly altered genes will be validated using RT-PCR with unique primers. Pearson product-moment analysis was performed on the two expression outcomes.
RESULTS: Three hundred forty-two up and 621 down-regulated cDNAs were considered unique to the treatment groups. Eighty-four percent of the variability in gene expression could be accounted for by the potent effects of amphotericin B/DOC. However, 15.4% of the variability was attributed to DOC alone. Calcium channel (α 1G), hemeoxygenase (decycling) 2 and interleukin-8 were significantly up-regulated. In addition, solute carrier family 4 anion exchanger, and glycogen synthase 2 (liver) were not significantly up regulated compared to media, but, were significantly up-regulated compared to the effects of amphotericin B/DOC.
CONCLUSIONS: These studies have identified a number of monocytic mRNA representing altered gene regulation associated with DOC. Further investigation should elucidate novel pathways involved in human toxicity.

142. Multi-center evaluation of community-acquired pneumonia: a focus on current treatment and outcome patterns in hospitalized patients. *Bonnie DeLor, Pharm.D., BCPS,* Thomas Wolfe, Pharm.D., Gary Buck, Pharm.D., Rick Dettloff, Pharm.D., BCPS, Tamara Evans, Pharm.D., BCPS, Martin Giannamore, Pharm.D., BCPS, Irene Orynchak, M.S., Kevin Townsend, Pharm.D., BCPS; Pfizer Inc., Detroit, MI; Pfizer Inc., Columbus, OH; Pfizer Inc., Indianapolis, IN; Pfizer Inc., Grand Rapids, MI; Pfizer Inc., Cleveland, OH; Pfizer Inc., Ann Arbor, MI.

PURPOSE: This multi-centered project evaluated the management of patients with community acquired pneumonia (CAP) among 20 institutions for the purpose of comparing CAP management to established guidelines and understanding current practices relative to treatment and outcomes.
METHODS: A retrospective chart review was conducted on 840 randomly selected patients with a discharge diagnosis of CAP admitted between October 1, 2000 and April 30, 2001. A standardized database was utilized to extract patient demographic and clinical data.
RESULTS: Pneumonia Severity Index (PSI) risk class I-II comprised 36% of hospital admissions for CAP. Overall mortality (2.2%) and length of stay (LOS) [mean ± SD, 5.2 ± 4.4 days] increased with increasing PSI risk classification (p<0.002). There were no significant LOS differences in the 7 most prevalent empiric regimens (which comprised 73.1% of all regimens). Patients switched to oral therapy had a longer LOS (5.9 vs. 4.6 days) [95% CI, 0.59-1.85, p<0.001] and had higher PSI risk scores (p<0.02). Time to first dose of antibiotic was 5 hours (3.4 vs. 8.4 hours) shorter if given in the emergency department (ED) (95% CI, 3.41-6.66, p<0.001). Initial empiric antibiotic regimen was changed in 34.5% of patients. The most common reason was a change from the ED regimen (33.4%).
CONCLUSIONS: Based on PSI risk classification, approximately one-third of the population was eligible for outpatient treatment. Longer LOS in patients switched to oral therapy may partially be related to a higher acuity of illness within this group. Initial doses of antimicrobials were more likely to be given on time when administered in the ED.

143. A trough-only vancomycin monitoring program at a university teaching hospital. *Laurel S. Fields, Pharm.D., M.S., BCOP,* Joseph S. Bubalo, Pharm.D., BCOP, BCPS, Daniel R. Touchette, Pharm.D., M.A., Karen B. Farmer; Oregon State University at Portland; Oregon Health & Science University, Portland, OR.

PURPOSE: Vancomycin monitoring standards vary widely in the literature and at Oregon Health & Sciences University (OHSU). Objectives were to 1) evaluate the effectiveness of a formalized vancomycin trough-only monitoring program against current practice and 2) evaluate program safety, therapeutic, and pharmacoeconomic outcomes.
METHODS: Clinical pharmacists prospectively recommended trough-only vancomycin levels and monitored patients using a standardized dosing and monitoring tool. This intervention group was compared to a historical control. Medical history, initial vancomycin regimen & monitoring parameters, vancomycin rationale, age, serum creatinine, concurrent nephrotoxic medications, and in-hospital course were recorded. Interventions, physician acceptance, vancomycin therapeutic outcomes, and safety data were

evaluated.
RESULTS: Ninety-eight trough-only and 135 control patients were enrolled from several wards, including BMT, ICU, and internal medicine. Demographic data were not different between the groups. The trough-only program was equally effective compared with the control group. An average 2.3 vs. 3.3 total serum concentrations ($p<0.001$) and 0.4 vs. 1.3 peak concentrations were drawn per patient respectively ($p<0.001$). Time from the first dose to the first vancomycin concentration was 2 vs. 1.5 days ($p<0.001$). Physicians accepted 97% of the interventions. The trough-only program averaged $271/patient vs. $307/control patient. No nephrotoxicity was attributable solely to vancomycin. The trough-only monitoring program resulted in equivalent outcomes; detailed analysis will be presented.
CONCLUSIONS: A trough-only vancomycin monitoring program resulted in statistically fewer vancomycin levels without affecting either safety or therapeutic outcomes throughout the adult hospital population. This program offers equally effective vancomycin monitoring with fewer laboratory draws, increased pharmacist involvement, and institutional savings.

144E. Hospital demographics and prevalence of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium*. *Kevin W. Garey, Pharm.D.,* Katie Suda, Pharm.D., Vikas Gupta, Pharm.D., Alisa Goetz, Pharm.D., Jennette Tran, Pharm.D.; University of Houston, Houston, TX; University of Illinois, Chicago, IL; Cardinal Health Provider Services, Houston, TX.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

145E. Regional variation in Gram-positive antimicrobial susceptibility patterns from non-teaching hospitals throughout the United States. Kevin W. Garey, Pharm.D., Katie Suda, Pharm.D., *Vikas Gupta, Pharm.D.,* Alisa Goetz, Pharm.D., Jennette Tran, Pharm.D.; University of Houston, Houston, TX; University of Illinois, Chicago, IL; Cardinal Health Provider Services, Houston, TX.

Presented at the 12th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America, Salt Lake City, UT, April 6-9, 2002.

146E. Evaluation of medication cost among community-acquired pneumonia and hospital-acquired pneumonia in community hospitals throughout the United States. *Katie J. Suda, Pharm.D.,* Vikas Gupta, Pharm.D., BCPS, Juanita Hill, R.Ph., Larry H. Danziger, Pharm.D.; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

147. Sequential intravenous to oral moxifloxacin monotherapy for community-acquired pneumonia. *Charles Fogarty, M.D.,* Scott Larsen, M.D., Timothy Jackson, M.D., Kamal Hamed, M.D., James Song, Ph.D., Deborah Church, M.D.; Lung and Chest Medical Associates, Spartanburg, SC; Fusion Clinical Trials, Red Bank, NJ; Tri-State Medical Group, Beaver, PA; Bayer Corp, West Haven, CT.

PURPOSE: In a prospective, randomized, open label study, the safety and efficacy of monotherapy with IV/PO moxifloxacin (MXF) was compared to therapy with a third-generation cephalosporin/macrolide combination (CMC) in patients with community-acquired pneumonia (CAP).
METHODS: Patients with CAP received either: 7-10 days of IV/PO MXF 400/400 mg QD or 7-10 days of IV ceftriaxone 2 gm QD ± IV/PO azithromycin (AZY) 500 mg on day 1 followed by IV/PO AZY 250 mg QD for 4 days for non-hospitalized patients, or IV AZY 500 mg QD for 2 days followed by IV/PO AZY 500 mg QD for 7-days for hospitalized patients. At discretion of investigator, patients were switched to PO cefuroxime axetil 500 mg BID ± PO AZY (as above). CMC comparator group received IV or PO metronidazole 500 mg Q6H for suspected aspiration pneumonia. Primary efficacy measure was clinical response at test-of-cure visit (TOC) 7-14 days post-therapy. Bacteriological response at TOC was the secondary efficacy measure. Adverse events were recorded for the intent-to-treat population.
RESULTS: Clinical success rates for the efficacy-valid population were 83% (90/108) for MXF- and 80% (90/113) for CMC-treated subjects at the TOC visit. Respective bacteriological response rates (confirmed + presumed eradication) were 82% (14/17) and 63% (15/24). Drug-related adverse events were reported in 18% (30/167) MXF- and 16% (27/168) CMC-treated patients.
CONCLUSION: Monotherapy with IV/PO MXF 400 mg QD was as effective and safe as CMC therapy in the treatment of CAP. Monotherapy with MXF represents a convenient alternative to combination therapy for the treatment of CAP.

148E. In vitro susceptibility of bloodstream candidiasis in cancer patients: correlation with outcome of antifungal therapy. *Russell E. Lewis, Pharm.D.,* Anastasia Antonidou, M.D., Harrys A. Torres, M.D., John Thornby, Ph.D., Jeffery Tarrand, M.D., Dimitrios P. Kontoyiannis, M.D., Sc.D.; University of Houston; University of Texas, Houston, TX.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

149E. In vitro susceptibility and tolerance of aspergillus species in a tertiary care cancer center: correlation with invasive aspergillosis and its outcome. *Russell E. Lewis, Pharm.D.,* Harrys A. Torres, M.D., John Thornby, Ph.D., Darshana P. Uphadyaya, Dimitrios P. Kontoyiannis, M.D., Sc.D.; University of Houston; University of Texas, Houston, TX.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

150E. Amphotericin B in systemic fungal infections: meta-analysis of conventional versus lipid formulations. *Stacey S. MacAulay, Pharm.D.,* Janet E. Martin, Pharm.D., Kelly B. Zarnke, M.D.; London Health Sciences Center, London, ON, Canada.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

151E. Efficacy of a new chromatography-based IGIV (10% formulation) on validated sinopulmonary infections in primary immune deficiency. *Harry Schroeder, M.D.,* Melven Berger, M.D., Anita T. Gewurz, M.D., Phillip Korenblat, M.D., Chaim Roifman, M.D., Ricardo Sorensen, M.D., Donald Stark, M.D., Mark Stein, M.D., Gordon Sussman, M.D., John Kelleher, M.D.; University of Alabama, Birmingham, AL; Rainbow Babies and Children's Hospital, Cleveland, OH; University Consultants for Allergy and Immunology, Chicago, IL; Clinical Research Center, LLC, St. Louis, MO; Hospital for Sick Children, Toronto, ON, Canada; Louisiana State University, New Orleans, LA; Allergy Associates of the Palm Beaches, North Palm Beach, FL; Wellesley Central Hospital, Toronto, ON, Canada; Bayer Corporation, West Haven, CT.

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152E. Rapid enveloped virus inactivation by caprylate: a robust solvent-detergent alternative. *Marina Korneyeva, Ph.D.,* Joann Hotta, Ph.D., Scott Rosenthal, Ph.D., Wytold Lebing, M.S., Dominique Pifat, Ph.D., Steve Petteway, Ph.D.; Bayer Corporation, Research Triangle Park, NC; Bayer Biological Products, Clayton, NC.

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153E. Process for a new intravenous immunoglobulin featuring caprylate virus inactivation and column chromatography. *Wytold Lebing, M.S.,* Ann Davis, B.S., Hanns-Ingolf Paul, Ph.D.; Bayer Biological Products, Clayton, NC; Bayer AG, Leverkusen, Germany.

Published in J Allergy Clin Immunol, January 2002;109:Part 2, No. 1.

155E. Penetration of meropenem into human skin blister fluid. *Dana Maglio, Pharm.D.,* David P. Nicolau, Pharm.D., FCCP, Renli Teng, Ph.D., Per T. Thyrum, M.D., Ph.D.; Hartford Hospital, Hartford, CT; AstraZeneca Pharmaceuticals, Wilmington, DE.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

156E. Pharmacodynamic profile of daptomycin against *Enterococcus faecalis* and methicillin-resistant *Staphylococcus aureus* in a murine thigh infection model. *Prachi K. Dandekar, Pharm.D.,* Pamela R. Tessier, M.S., Peter Williams, M.D., Charles H. Nightingale, Ph.D., David P. Nicolau, Pharm.D., FCCP; Hartford Hospital, Hartford, CT.

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157. The influence of pH on the susceptibility of candida bloodstream isolates against fluconazole, itraconazole, and voriconazole. *Manjunath P. Pai, Pharm.D.,* Renee-Claude Mercier, Pharm.D.; University of New Mexico, Albuquerque, NM.

PURPOSE: This study evaluated the influence of two clinically relevant (urine, blood) pH values on the minimum inhibitory concentration (MIC) of fluconazole (Flu), itraconazole (Itr) and voriconazole (Vor) against Candida species.
METHODS: Twenty-two clinical candida bloodstream isolates and 2 ATCC® strains 6258 (*C. krusei*), and 22019 (*C. parapsilosis*) were assessed. MICs were performed in duplicate by broth microdilution against Flu (0.25-128 µg/mL), Itr (0.008-4 µg/mL) and Vor (0.008-4 µg/mL) using the NCCLS M27-A procedure using MOPS-buffered RPMI adjusted to pH 7.0 (Med7, standard media), pH 7.45 (Med7.45), and pH 6.0 (Med6). MICs were determined at 24 and 48 hours (H) based on a prominent reduction in turbidity.
RESULTS: The number of isolates, and 48H MIC_{90} (µg/mL) for Flu, Itr,and Vor respectively using Med7 were: *C. albicans* (n=16, 1.0, 0.06, 0.06), *C. glabrata* (n=5 , 16.0, 2.0, 0.25), *C. parapsilosis* (n=2, 2.0, 0.25, 0.03), *C. krusei* (n=1, 16.0, 0.5, 0.25). The 24H MICs were typically within 1-dilution of the 48H MIC values. The 48H MICs of Flu, Itr, and Vor were within 1-dilution when testing *C. albicans, C. parapsilosis, C. krusei* in Med7, Med7.45, and

Med6. However, the 48H MICs of Flu, Itr, and Vor were 2-dilution higher in Med6 and 2-dilution lower in Med7.45 compared to Med7 against *C. glabrata*.
CONCLUSIONS: The MICs of Flu, Itr, and Vor are higher at pH 6.0 and lower at pH 7.45 compared to media at pH 7.0 when testing *C. glabrata*. The influence of pH should be considered when developing pharmacodynamic models that use *C. glabrata*.

158. Relationship between antimicrobial usage and prevalence of Gram-negative bacterial resistance at a teaching hospital in southern Thailand. *Sutthiporn Pattharachayakul, Pharm.D., BCPS*; Prince of Songkla University, Songkhla, Thailand.

PURPOSE: The purpose of this study was to assess the relationship between antimicrobial usage and prevalence of gram negative bacterial resistance.
METHOD: Antimicrobial usage including ceftazidime, imipenem, gentamicin, ciprofloxacin and cefoperazone/sulbactam were collected annually from 1998 to 2000. The amount of antimicrobial usage in gram was converted into defined daily dose (DDD)/1000 patient-days. Prevalence of antimicrobial resistance of 5 common hospital acquired gram negative bacteria including *Acinetobacter baumanii, Pseudomonas aeruginosa, Escherichia coli, Enterobacter cloaceae* and *Klebsiella pneumoniae* were collected from 1999-2001. Correlation between antimicrobial usage and prevalence of Gram-negative bacterial resistance were assessed statistically using the Spearman Rank Correlation Analysis (SPSS System for Windows v 7.5)
RESULTS: There was a significant correlation between ceftazidime usage and prevalence of ceftazidime resistant *P. aeruginosa, E. coli , A. baumanii* and *K. pneumoniae* (r=1, p=0.00). In addition, we found a significant correlation between ciprofloxacin usage and prevalence of ciprofloxacin resistant *A. baumanii* and *P. aeruginosa* (r = 1, p=0.00), as well as imipenem usage and the prevalence of imipenem resistant *P. aeruginosa* (r = 1, p=0.00).
CONCLUSIONS: Since there was a strong relationship between some antibiotic usage and the prevalence of gram negative antimicrobial resistance, the strategy to control the use of those antimicrobial agents is needed.

159E. National survey of antifungal susceptibility testing practices in community hospitals throughout the United States. *Katie J. Suda, Pharm.D.,* Manjunath (Amit) P. Pai, Pharm.D., Vikas Gupta, Pharm.D., BCPS, John P. Quinn, M.D., Susan L. Pendland, Pharm.D.; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX; University of New Mexico, Albuquerque, NM.

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160E. National survey of extended-spectrum β-lactamase susceptibility testing practices in community hospitals throughout the United States. *Katie J. Suda, Pharm.D.,* Vikas Gupta, Pharm.D., BCPS, John P. Quinn, M.D., Susan L. Pendland, Pharm.D.; University of Illinois at Chicago, Chicago, IL; Cardinal Health Provider Pharmacy Services, Houston, TX.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

161E. Heat-induced super-aggregation of amphotericin B attenuates its ability to induce cytokine and chemokine production in the human monocyte cell line THP-1. *P. David Rogers, Pharm.D., Ph.D.,* Katherine S. Barker, Ph.D., Vanessa Herring, B.S., Melissa Jacob, Ph.D.; University of Tennessee, Memphis, TN; University of Mississippi, Oxford, MS.

Presented at the 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

162E. Pneumolysin-dependent cytokine and chemokine production in THP-1 cells exposed to *Streptococcus pneumoniae*. *P. David Rogers, Pharm.D., Ph.D.,* Justin Thornton, B.S., Katherine S. Barker, Ph.D., Edwin Swiatlo, M.D., Ph.D., Larry S. McDaniel, Ph.D.; University of Tennessee, Memphis, TN; University of Mississippi Medical Center, Jackson, MS.

Presented at the 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

163. Functional genomic analysis of coordinate gene expression in stepwise acquisition of high level azole antifungal resistance in *Candida albicans*. *P. David Rogers, Pharm.D., Ph.D.,* Katherine S. Barker, Ph.D.; University of Tennessee, Memphis, TN.

PURPOSE: The purpose of this study was to identify genes that contribute to azole antifungal resistance by examining differential gene expression on a genomic scale throughout the stepwise acquisition of this phenotype.
METHODS: Four isogenic, serial, clinical isolates of *C. albicans* were obtained from an AIDS patient with oropharyngeal candidiasis who failed fluconazole therapy (isolates 2, MIC=0.25 µg/mL; 3, MIC=4 µg/mL; 15, MIC=16 µg/mL; and 17, MIC>64 µg/ml). RNA was isolated for cDNA microarray analysis. Gene expression profiles for isolates 3, 15 and 17 were compared to that of isolate 2.
RESULTS: As expected, CDR1 and CDR2 were up-regulated only in isolate 17, whereas MDR1 was up-regulated in isolates 3, 15 and 17. Among the 11 additional genes up-regulated in isolate 17 were 4 genes coordinately regulated with CDR1/2 (ERG2, GPX1, LTV1, RTA3) and 7 coordinately regulated with MDR1 (GRP2, IFD1, IFD4, IFD5, IFD7, MAL31, IPF5987). Among the 111 genes down-regulated in isolate 17 were 15 genes coordinately regulated with CDR1/2 (EBP1, CDK2, DAL5, ODC1, PFZ1, SPO72, SUR2, and 7 unknown) and 4 coordinately down-regulated with MDR1 (FET34, SOD1, and 2 unknown). Other down-regulated genes included glutathione pathway genes (GTT2, IPF11526), chitin synthase genes (CHS1, CHS4), and agglutinin-like protein genes (ALS2, ALS3, ALS9).
CONCLUSIONS: These results implicate a multitude of gene products in azole resistance. Furthermore, they demonstrate the coordinate expression of the IFD family of aryl-alcohol dehydrogenase enzymes with the MDR1 efflux pump, and the ergosterol biosynthesis enzyme, C-8 sterol isomerase, as well as the glutathione pathway with the CDR efflux pumps.

164. Surgical antimicrobial prophylaxis: administration timing analysis. *Eileen M. Sakai, Pharm.D.*; Pharmacy Healthcare Solutions, Grapevine, TX.

PURPOSE: This study identifies the key steps that can influence the timing of the preoperative antibiotic (Pre-Op Abx.) administration in surgical patients.
METHODS: The medical records of 130 contaminated or clean/contaminated procedures in October 2000 were reviewed. The type of patient, timing of drug allergy documentation, timing of Pre-Op Abx. ordering and administration, name/dose of Pre-Op Abx., and location/point person for Pre-Op Abx. administration were documented.
RESULTS: The surgical procedures were performed in 36% In-Pt, and 64% in Ambt-Pt. Pre-Op Abx. administration timings resulted in 10.3% "Early" (>120 minutes prior to incision); 44.8% "On-Time" (30-120 minutes prior to incision); 38% "Late" (<30 minutes prior to or after incision); and 6.9% "Not given". The allergy documentation and Pre-Op Abx. ordered rates were 77.8% and 44.4% for "Early"; 69.7% and 63.6% for "Late"; compared to 89.7% and 87.2% for "On-Time". "On-Time" administration was highest when allergy documentation and Pre-Op Abx. Ordering were done prior to surgery date - 51.5% and 52.5% respectively. The "Late" was the highest when allergy documentation and Pre-Op Abx. Ordering was not done prior to surgery date - 55.6% and 54.5% respectively. The majority of "On-Time" doses were administered in the Preoperative Holding Unit; all of the "Late" doses were given in OR. The storage location of the antibiotics did not make a difference in administration timing. The antibiotics with longer required infusion time were more prone to be "Late". Diffused responsibility for antibiotic administration in Preoperative Holding Unit added to the delay of the administration timing.
CONCLUSION: The timing of patients' drug allergy documentation and Pre-Op Abx. Ordering indicated a clear correlation to the Pre-Op Abx. administration timing in surgical patients. With optimal Pre-Op Abx. administration timing being one of the key factors in preventing Surgical Wound Infections, recognition of the importance of Pre-Op Abx. administration timing by surgeons and anesthesiologists is imperative in order to make a difference in their practice pattern.

165. Susceptibility of *S. pneumoniae* to ketolides, macrolides, azithromycin, and clindamycin in North America, 1996-2002, with subanalysis based on test methodology. *Kevin A. Enzweiler, Pharm.D.,* John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To compare activity of macrolides (M), ketolides (K), azithromycin (A), and clindamycin (C) against *S. pneumoniae* (SP) using an integrated database of MIC studies.
METHODS: We assessed susceptibility (S) to 6 drugs, including K [telithromycin (T) and ABT-773 (AB)] using a database of published studies (n=61). Isolates were divided into penicillin S, macrolide S, and resistance phenotypes (*mef* or *erm*). Weighted geometric mean MIC_{90}s (GMIC) were calculated for each drug/organism/year and changes over time noted. The multicenter nature of many studies precluded a meaningful analysis of inter-regional variations. Variations based upon methodology and test conditions were sought.
RESULTS: The categories of SP for which there were data for most of the years studied were those based on penicillin S. For these, GMICs of pen-intermediate and -resistant SP increased over the time period studied for A, erythromycin and C, but not with clarithromycin. K were active against various categories of M resistance.

	Weighted geometric mean MIC_{90} (µg/ml) for Year 2001				
Drug	# isolates	mef E	mef A	erm B	ery R
Telithromycin	100-403	0.50	0.06	0.03	0.14
ABT-773	23-346	0.13	0.03	0.03	0.10
Clindamycin	82-131	1	0.09	52	64
Azithromycin	103-346	7	8	256	68
Clarithromycin	103-128	7	4	256	NA
Erythromycin	23-203	5	5	182	64

No differences were detected based on methods or conditions although only 4% and 20% of the data, respectively, reflected use of E-test and agar dilution.

CONCLUSIONS: From this analysis utilizing a large database of 61 studies, K appear more potent against SP than the other agents evaluated, including those isolates resistant to M, A and C.

166. Percent susceptible vs. percent resistant: should both markers be used in surveillance of susceptibility trends? *Kevin A. Enzweiler, Pharm.D.,* John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To determine if % resistance (%R) is a more sensitive marker than % susceptible (%S) in the assessment of susceptibility trends
METHODS: Nine years of aggregate susceptibility data (1992-2000) for 5 Gram-positive and 8 Gram-negative organisms against 29 antimicrobials from our hospital were analyzed: hospital-wide, ICU, and non-ICU areas for which each quarter had at least 10 isolates reported. Annual susceptibility data for all culture sites were analyzed by linear regression. Only those data sets (same organism, same drug, same hospital area, same culture site) with relatively strong relationships ($R^2 \geq 0.5$) for either %S or %R vs. time were further analyzed. To compare the strengths of the relationships, the ratio of R^2 (%R value / %S value) was determined. Instances when R^2 for %R vs. time was 20% stronger or weaker (determined by the R^2 ratio >1.2 or < 0.8) than that for % S vs. time were assessed.
RESULTS: 36 relationships (drug/organism pairs) met the criteria for final analysis (4 Gram-negative and 2 Gram-positive organisms; 9 drugs, including 5 beta-lactams, hospital-wide and Non-ICU areas, non-urine and all combined culture sites). With these relationships, use of %R provided a stronger relationship in 76% of the comparisons while it was associated with a weaker relationship in 24% of instances. Importantly, 8 strong relationships detected when considering %R (e.g., ceftazidime and *E. cloacae*) were not detected when using %S, while 3 strong relationships were found when considering %S data but not when using %R.
CONCLUSIONS: Sole reliance on the use of %S as a marker of bacterial susceptibility may fail to detect important trends in susceptibility. It may be prudent to evaluate both %S and %R when evaluating susceptibility trends.

167. Declining microbial susceptibility to fluoroquinolones in North America, Europe, and Asia: analysis of 204 studies from 1982 to 2002. *Kevin A. Enzweiler, Pharm.D.,* John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To analyze changes in bacterial susceptibility (S) to fluoroquinolones (FQs) over time using a database of published studies with subanalysis by geographical region, drug and organism.
METHODS: We assessed S trends for 13 G - and 7 G + organisms against ciprofloxacin (CIP), levofloxacin (LEV), gatifloxacin (GAT), moxifloxacin (MOX), gemifloxacin (GEM), and garenoxacin (GAR) in North America (NA), Europe (EU) and Asia (AS). Using criteria of ≥ 3 studies over at least 3 years with ≥ 20 isolates per year, linear regression of the log of the weighted geometric mean MIC_{90} (weighting based on number of isolates) vs. time was performed for each organism/drug pair. Each was categorized by direction of its regression line slope [positive (pos) or negative] and analyzed by logistic regression. The subsets of pos (↑ MICs) and steepest pos slopes (≥ 0.6) were analyzed with ANOVA for slope differences. The rate of occurrences of pos and steepest pos slopes (rate) for each region, drug, and organism was calculated (% observed in the subset / % possible).
RESULTS: Of the 360 possible relationships involving 398,487 drug/organism pairs, 45% (n = 154) met our criteria with 65% (100/154) having pos slopes. EU had the highest rate of pos slopes (rate = 1.1), although AS and NA had higher mean slopes and higher rates of steepest pos slopes at 1.5 and 1.2, respectively ($p > 0.05$ among the regions). CIP, MOX, and GEM had a greater rate of pos slopes compared to LEV ($p < 0.02$); GEM and GAT had both higher mean slopes ($p < 0.03$ compared to LEV, CIP) and a higher rate of steepest pos slopes (rate = 3.4, 2.5 respectively). G – and G + organisms were equally likely to have pos slopes; however, G – organisms had a higher rate of steep pos slopes (rate = 1.2) with *E. coli* the G – organism most likely to have pos (rate =1.4; $p < 0.04$ vs. 7 organisms) and steep pos slopes (rate = 3.0).
CONCLUSIONS: Increases in MICs were found for a majority of relationships with the most dramatic increases frequently involving newer FQs and G-organisms.

168. Comparison of quarterly, semi-annual, and annual data for use in susceptibility trend analysis. *Kevin A. Enzweiler, Pharm.D.,* John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To compare the impact of quarterly, semi-annual, and annual susceptibility data on the analysis of susceptibility trends.
METHODS: Quarterly (Q), aggregate, non-urine susceptibility data from 9 years (1992-2000) for 5 Gram-positive (G+) and 8 Gram-negative (G-) organisms at our institution were collected for hospital-wide, ICU, and non-ICU areas. Semi-annual (S) and annual (A) susceptibility data for all culture sites were calculated from Q data and all were analyzed vs. time by linear regression. Q, S, and A %S or %R were calculated only for those sets (same organism, same drug, same hospital area) for which each quarter had at least 10 isolates. Agreement in slopes (same direction of the regression line) within each of the %S or %R data sets among time periods and differences in the strengths of the relationships (R^2) among the time periods were determined.
RESULTS: 184 sets met the criteria for final analysis (5 G- and 4 G + organisms; 16 drugs, hospital-wide and Non-ICU areas). In 98% of the sets, the 3 time periods showed agreement with the direction of the susceptibility trend slopes. Only four instances of disagreement in susceptibility trends were found (2 A vs. S&Q, 1 S vs. A&Q, and 1 Q vs. A&S) which were weak relationships (all $R^2 < 0.03$). The rank order of relationship strength was A > S > Q in 89% of the sets with 24%, 11%, and 3%, respectively, having R^2 values >0.5. Only 32 instances (within 20 sets) involved larger R^2 in the shorter time period (all $R^2 < 0.4$). Of these, 34% were Q > A, 19% were Q > S, and 47% were S > A.
CONCLUSIONS: In most instances, %S and %R trends agreed among the different time periods but had stronger relationships over time when considering longer time periods. The desired strength of the relationships may be the determining factor in choosing which time period to use in the analysis of susceptibility trends.

169. Moxifloxacin in the treatment of community-acquired pneumonia associated with drug-resistant *Streptococcus pneumoniae*. Charles Fogarty, M.D., *Shurjeel Choudhri, M.D.,* Janet Herrington, M.S., Barbara Painter, Ph.D., Renee Perroncel, B.A., Deborah Church, M.D.; Lung and Chest Medical Associates, Spartanburg, SC; Bayer Corporation, West Haven, CT.

PURPOSE: There has been a dramatic increase in infections due to penicillin resistant (PRSP) and penicillin plus macrolide resistant (DRSP) *S. pneumoniae* in the US. The objective of this study was to determine the efficacy of moxifloxacin (MXF) in the treatment of community-acquired pneumonia (CAP) due to PRSP and DRSP.
METHODS: Patients with CAP due to penicillin sensitive *S. pneumoniae* (PSSP), PRSP and DRSP were identified from an ongoing prospective, open, non-comparative, multi-center, multinational trial. All patients received oral MXF 400 mg QD for 10 days. The primary endpoint was clinical success at the test-of-cure (TOC) visit (10-14 days post-therapy) for patients who had an initial sputum or blood culture positive for *S. pneumoniae*. MXF, penicillin, erythromycin, clarithromycin, and azithromycin MICs were determined by microbroth dilution.
RESULTS: The study identified 55 patients with CAP due to *S. pneumoniae* including 42 patients with PSSP, 3 patients with PRSP and 10 patients with DRSP. All *S. pneumoniae* isolates, PSSP, PRSP and DRSP were highly susceptible to MXF (MIC range: 0.06-0.25 mg/l). The clinical cure rate at TOC was 98% (41/42), for PSSP, 100% (3/3) for PRSP and 100% (13/13) for DRSP.
CONCLUSIONS: Most (77%) PRSP strains were also resistant to all macrolides tested. All PSSP, PRSP, and DRSP strains isolated remained highly susceptible to MXF. Moxifloxacin was highly efficacious in the treatment of CAP due to PRSP and DRSP and represents an excellent choice for the treatment of CAP due to *S. pneumoniae*.

170E. Safety of moxifloxacin in the elderly. Vincent Andriole, M.D., *Shurjeel Choudhri, M.D.,* Daniel Haverstock, M.S., Deborah Church, M.D.; Yale University, New Haven, CT; Bayer Corporation, West Haven, CT.

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172. Pharmacodynamic evaluation of meropenem and imipenem against *Pseudomonas aeruginosa* and enterobacter species using Monte Carlo analysis. *David S. Burgess, Pharm.D.,* Michael B. Kays, Pharm.D., Gerald A. Denys, Ph.D.; University of Texas Health Science Center, San Antonio, TX; Purdue University, Indianapolis, IN; Clarian Health Partners, Methodist Hospital, Indianapolis, IN.

P. aeruginosa (PSA) and Enterobacter species are the most common gram-negative pathogens in hospital-acquired pneumonia. For β-lactams, treatment outcomes have been linked to the time (%) that drug concentrations remain above the MIC of a pathogen (T>MIC).
PURPOSE: To compare the pharmacodynamic profiles of meropenem and imipenem against recent clinical isolates of PSA and Enterobacter species using Monte Carlo analysis.
METHODS: MICs were determined by broth microdilution (NCCLS) for 158 PSA isolates and 116 Enterobacter isolates (*E. cloacae*, 83; *E. aerogenes*, 33). All organisms were isolated from infected patients at Methodist Hospital in Indianapolis, IN, and duplicate isolates were excluded. Pharmacokinetic parameters were obtained from healthy volunteer studies, and a 5,000 patient Monte Carlo simulation was performed for meropenem (0.5 g q6h, 1 g q8h) and imipenem (0.5 g q6h, 1 g q6h) against the isolates. Data were analyzed for the probability of obtaining free T>MIC for 50% and 70% of the dosing interval.
RESULTS: For PSA, the MIC_{50}, MIC_{90}, and %S were 0.5 µg/ml, 8 µg/ml, and 88.6% for meropenem and 1 µg/ml, 16 µg/ml, and 80.4% for imipenem. For Enterobacter species, the MIC_{50}, MIC_{90}, and %S were 0.25 µg/ml, 0.25 µg/ml, and 100% for meropenem and 0.25 µg/ml, 1 µg/ml, and 100% for imipenem. For PSA, the probabilities of obtaining free T>MIC for 50% and 70% of the

dosing interval were 92% and 87% for meropenem 0.5 g q6h, 94% and 88% for meropenem 1 g q8h, 75% and 63% for imipenem 0.5 g q6h, and 83% and 74% for imipenem 1 g q6h. For Enterobacter species, the probabilities of obtaining free T>MIC for 50% and 70% of the dosing interval were 96% and 92% for meropenem 0.5 g q6h, 95% and 88% for meropenem 1 g q8h, 89% and 79% for imipenem 0.5 g q6h, and 92% and 85% for imipenem 1 g q6h.
CONCLUSIONS: Although the carbapenems exhibited similar susceptibility profiles, meropenem was the more potent agent and provided the best probability of obtaining free T>MIC for 50% and 70% of the dosing interval for both PSA and Enterobacter species. In addition, meropenem 0.5 g q6h provides the opportunity for a substantial reduction in daily drug cost compared to 1 g q8h and both imipenem dosing regimens.

173. Comparison of Vitek™ and broth microdilution methods for testing cefepime and ceftazidime against *Pseudomonas aeruginosa* and enterobacter species. Gerald A. Denys, Ph.D., Pam B. Renzi, MT(ASCP), *Michael B. Kays, Pharm.D.*; Clarian Health Partners, Inc.; Methodist Hospital; Purdue University, Indianapolis, IN.

Previous reports have documented high false-resistance rates for cefepime and *Pseudomonas aeruginosa* (PSA) using the Vitek™ susceptibility system. In January 1999, the manufacturer removed restrictions for testing this combination when using software version 7.01.
PURPOSE: To compare Vitek and broth microdilution (BMD) susceptibility results for cefepime and ceftazidime against PSA and Enterobacter species.
METHODS: Clinical, non-duplicate isolates of PSA (n=158) and Enterobacter species (n=116) recovered from infected patients in intensive care and general medical units at Methodist Hospital (Indianapolis, IN) were tested. Gram-negative Vitek susceptibility cards (GNS-125) were inoculated and incubated in the Vitek instrument according to manufacturer's recommendations. The cards were automatically read and analyzed by the Vitek computer (software version 7.01). BMD MICs were performed according to NCCLS guidelines (M7-A5). After inoculation, BMD panels were incubated for 18-20 hours at 35ºC, and MICs were read manually. NCCLS breakpoints were utilized, and differences between testing methods were determined by chi-square ($p<0.05$).
RESULTS: Cefepime and ceftazidime susceptibility results for PSA were significantly different by Vitek and BMD, but ceftazidime resistance was the same between methods. For Enterobacter, Vitek and BMD were significantly different for ceftazidime, with a higher resistance rate by BMD. Five ceftazidime-resistant Enterobacter strains were reported susceptible by Vitek (very major error rate, 4.3%).

	Susceptible (%)		Intermediate (%)		Resistant (%)		
	Vitek	BMD	Vitek	BMD	Vitek	BMD	p-value
Cefepime							
PSA	72.1	88.0	19.0	7.6	8.9	4.4	0.002
Enterobacter sp.	99.1	100.0	0.0	0.0	0.9	0.0	NS
Ceftazidime							
PSA	79.7	88.0	12.7	4.4	7.6	7.6	0.032
Enterobacter sp.	81.0	75.9	5.2	0.8	13.8	23.3	0.037

CONCLUSIONS: Vitek continues to produce erroneous susceptibility results for cefepime and PSA. Alternative susceptibility testing methods should be utilized when testing these agents against PSA and ceftazidime against Enterobacter species.

Nephrology

174. Effect of sevelamer hydrochloride and calcium acetate on the relative oral bioavailability of ciprofloxacin. Michael B. Kays, Pharm.D., *Brian R. Overholser, Pharm.D.*, Bruce A. Mueller, Pharm.D., Sharon M. Moe, M.D., Kevin M. Sowinski, Pharm.D.; Purdue University; Indiana University, Indianapolis, IN.

PURPOSE: The purpose of this study was to determine the effects of sevelamer HCl (Renagel®) and calcium acetate on the relative bioavailability of oral ciprofloxacin in healthy volunteers.
METHODS: Fifteen healthy subjects (8M, 7F) were enrolled. They were admitted to the research unit in the morning of each study day, and they were required to fast ≥ 8 hr prior to admission. Subjects were randomly assigned to receive each of the following regimens administered orally: ciprofloxacin 750 mg alone (Arm A); ciprofloxacin 750 mg + 7 sevelamer 403 mg capsules (Arm B); ciprofloxacin 750 mg + 4 calcium acetate 667 mg tablets (Arm C). The washout period between treatments was ≥ 7 d. Serial blood samples were obtained over a 24 hr period, and ciprofloxacin serum concentrations were determined by HPLC. Maximum serum concentrations (C_{max}) and time to C_{max} (T_{max}) were determined by visual inspection of the concentration-time curves. The area under the serum concentration-time curve from 0 to infinity (AUC) and terminal elimination half-life ($t_{1/2}$) of ciprofloxacin were estimated by non-compartmental analysis. The relative bioavailability of ciprofloxacin in arms B and C was calculated as $AUC_{Arm\ B\ or\ Arm\ C}/AUC_{Arm\ A}$. Statistical analysis was performed using Friedman's test and the Wilcoxon Signed Rank test ($p<0.05$), where appropriate.
RESULTS: Median (Range) data are shown below.

	Ciprofloxacin Alone	Ciprofloxacin + Sevelamer HCl	Ciprofloxacin + Calcium Acetate
C_{max} (µg/ml)[a]	3.77 (1.97 - 5.39)	2.49 (0.979-5.34)[b]	1.90 (1.23-3.01)[b,c]
T_{max} (hours)	1.50 (0.50-4.00)	1.18 (0.50-4.00)	2.00 (1.00-4.00)
AUC (µg*hr/ml)[a]	18.55 (14.24-32.02)	11.27 (4.50-28.17)[b]	10.81 (6.54-15.72)[b]
$t_{1/2}$ (hours)	5.38 (4.14-6.26)	5.18 (3.84-7.33)	5.04 (4.62-7.33)
Relative F[a]	1.00	0.52 (0.27-1.16)[b]	0.49 (0.33-0.89)[b]

[a]$p<0.05$ by Friedman's test
[b]$p<0.05$ by Wilcoxon Signed Rank test when compared to ciprofloxacin alone
[c]$p<0.05$ by Wilcoxon Signed Rank test when compared to ciprofloxacin + sevelamer

CONCLUSIONS: The relative bioavailability of ciprofloxacin was significantly decreased when co-administered with sevelamer HCl or calcium acetate. Concomitant administration of these drugs decreases serum ciprofloxacin concentrations and may reduce clinical efficacy or promote emergence of resistance to ciprofloxacin.

175. A randomized trial comparing two modalities of alteplase administration for treatment of occluded hemodialysis catheters. Jennifer M. MacRae, M.Sc., M.D., Gabriel Loh, B.Sc.Pharm., *Stephen Shalansky, Pharm.D.*, Mercedeh Kiaii, M.D.; St. Paul's Hospital, Vancouver, BC, Canada.

PURPOSE: To compare two alteplase regimens, differing only in dwell time duration, for use in occluded hemodialysis catheters resulting from suspected thrombus.
METHODS: Patients receiving hemodialysis via catheter between Oct./01 and May/02 with a blood pump speed (BPS) ≤ 250 mL/min after flushing and repositioning were included in the study if they had not been previously enrolled. Patients received 1 mg/mL alteplase (volume determined by the catheter lumen size) randomized to one hour dwell or dwell until the next hemodialysis session (48-72 hours). The primary endpoint was the proportion of patients achieving BPS > 250 mL/min upon alteplase aspiration, and the secondary endpoint was the same outcome assessed at two weeks after alteplase was first instilled.
RESULTS: Twenty-six patients were randomized to one hour dwell, and 34 patients to 48-72 hour dwell. The study groups were similar with respect to mean age (70 versus 67 years), gender (69% versus 56% male), and median baseline BPS (200 mL/min versus 211 mL/min). The primary endpoint was achieved in 16 (62%) of one hour dwell and 27 (79%) of 48-72 hour dwell patients ($p=0.13$), while the secondary endpoint was achieved in 12 (46%) and 19 (56%) patients, respectively ($p=0.46$). Of the catheters remaining dysfunctional at 2 weeks, dye studies indicated the cause to be persistent thrombus in 13/14 (93%) one hour dwell and 10/15 (67%) 48-72 hour dwell patients.
CONCLUSION: Although there was no statistically significant difference in the proportion of patients achieving adequate BPS, allowing alteplase to dwell until the next hemodialysis session appears to be technically easier and may be more effective.

176. A comparison of two dosage regimens of intravenous vancomycin in high flux hemodialysis patients. Curtis Harder, B.Sc.Pharm., *Stephen Shalansky, Pharm.D.*, Ron Werb, M.D., Joanne Jung, B.Sc.Pharm., Andria Lee, B.Sc.Pharm., Doson Chua, B.Sc.Pharm., Adeera Levin, M.D., Mercedeh Kiaii, M.D.; St. Paul's Hospital, Vancouver, BC, Canada.

PURPOSE: To compare the proportion of vancomycin treatment courses resulting in therapeutic steady state levels using two common dosing regimens in high flux hemodialysis patients.
METHODS: Patients received a loading dose of 25 mg/kg, then were randomized to receive a maintenance dose of either 500 mg every dialysis (q dialysis) or 20 mg/kg every second dialysis (q2 dialysis). The target therapeutic range was 10-20 mg/L.
RESULTS: Steady-state vancomycin serum levels were obtained in 21 of 28 q dialysis treatment courses and 17 of 31 q2 dialysis treatment courses. The main reason for dropout prior to reaching steady-state was changing to a less expensive antibiotic based on culture and sensitivity results. Demographics were similar between patients in the q dialysis group (17 patients) and q2dialysis group (16 patients), respectively, including mean weight (64 +/-9.7 vs. 59 +/-10 kg), sex (43% vs. 44% males) and mean age (67 +/-14 vs. 67 +/-15 years). Pre-steady state levels were more often in the target range in the q dialysis arm (89%) than the q2dialysis arm (25%, $p<0.001$); however, there was no statistically significant difference in the proportion of treatment courses resulting in therapeutic steady state serum levels (95% vs. 76% respectively, $p=0.152$). Clinical cure was eventually achieved on vancomycin in 95% (20/21) q dialysis and 94% (16/17) q2dialysis treatment courses ($p=1.0$).
CONCLUSION: Although there was no statistically significant difference in the proportion of treatment courses resulting in therapeutic steady state levels between the two regimens, the q dialysis regimen maintained therapeutic levels more consistently throughout the course of vancomycin therapy.

177. Assessment of outcomes of intradialytic parenteral nutrition. Nancy Cherry, B.Sc., *Karen F. Shalansky, Pharm.D.*; Vancouver General Hospital, Vancouver, BC, Canada.

PURPOSE: Patients with end-stage renal disease often suffer from

malnutrition. One modality used to treat malnourished hemodialysis patients is intradialytic parenteral nutrition (IDPN), a multi-component nutritional supplement. The primary outcome of this trial was to determine the effects of IDPN on weight and serum albumin in a large tertiary care institution.
METHODS: All patients who received IDPN for greater than 1 month from program inception in June 1997 to December 2000 were analyzed. Patients received IDPN as amino acid 10% 250 ml or 500 ml, dextrose 50% 250 ml and fat emulsion 20% 250 ml. IDPN was administered during each hemodialysis run three times weekly. Data was collected at 6 and 3 months prior to IDPN administration as well as at baseline, 3, 6, 9, and 12 months post-therapy. Therapeutic efficacy was assessed by percent change from baseline of dry weight and serum albumin.
RESULTS: Twenty-six courses of IDPN in 24 patients met inclusion criteria. The mean duration of treatment was 4.3 months. A significant decline in dry weight was observed at both 6 and 3 months prior to IDPN initiation. Dry weight increased from baseline and achieved significance at 6, 9, and 12 months post-therapy. Serum albumin also significantly improved from baseline at 3 and 9 months. Compared to baseline, there was a 3- to 4-fold increase in the percent of patients with serum albumin greater than or equal to 34 g/L. Adverse drug reactions consisted primarily of excess fluid gain and hyperglycemia.
CONCLUSION: IDPN significantly increases both weight and serum albumin in malnourished hemodialysis patients.

178E. In vitro assessment of influence of molecular weight on drug clearance by conventional and synthetic dialyzers. *Gary R. Matzke*, Paul M. Palevsky, Reginald F. Frye; University of Pittsburgh; VA Pittsburgh Healthcare System, Pittsburgh, PA.

Presented at the 31st Annual Meeting of the American College of Clinical Pharmacology, San Francisco, CA, September 21-23, 2002.

179. Prevalence of anuria in neonates receiving enalaprilat therapy. *John E. Emanuel, M.S., Pharm.D.*, Renee F. Robinson, Pharm.D., Milap C. Nahata, Pharm.D., John Hayes, Ph.D., John D. Mahan, M.D.; Ohio State University; The Children's Hospital Research Institute, Columbus, OH.

PURPOSE: Determine the safety of enalaprilat and enalapril maleate in the treatment of neonatal hypertension addressing possible anuria and renal failure reported with angiotensin converting enzyme inhibitors [hypotensive effects and alterations in renal perfusion].
METHODS: Medical records of all neonates who received enalaprilat or its prodrug, enalapril maleate, over 30 months (1999-2001) were reviewed. Demographic information, complications during pregnancy, comorbid conditions, and catheter utilization (UAC) were obtained. Dose and route of enalaprilat, concurrent medications, clinical and laboratory parameters were obtained. Data were analyzed via the proc mixed model to account for variability. Pearson's product-moment correlation coefficient was used to assess the relationship between urine output, and blood pressure.
RESULTS: Gestational age at admission was 254 ± 56 days and the start of therapy was 269 ± 58 days. Duration of therapy was 8 ± 11 days with an average of 8 ± 9 doses. APGAR scores were 4 ± 3 at 1 minute and 6 ± 3 at 5 minutes. Eighteen patients (n=27) had a UAC, 14 received enalaprilat, nine enalapril maleate and four both. Proc mixed model confirmed no change in urine output (F=0.26, p=0.77 with 2, 49 degrees of freedom). Urine output correlated with systolic blood pressure (r=0.42, p=0.001), and diastolic blood pressure (r=0.365, p=0.008). Urine output did not correlate with mean arterial pressure (r=0.239), heart rate (r=0.08), blood urea nitrogen (r= -0.037) or serum creatinine (-0.035).
CONCLUSIONS: No difference was found in urine output during therapy when appropriate monitoring was performed. Appropriate dose adjustment and monitoring is required for the safe utilization of enalaprilat in this population.

180E. The influence of dialyzer type on serum albumin in hemodialysis patients. Kalai C. Parthiban, M.D., *Michael H. Schwenk, Pharm.D.*, Winicjusz Palecki, M.D., Carl R. Rosenberg, Ph.D., Marilyn Galler, M.D.; New York Hospital Medical Center of Queens, Flushing, NY.

Presented at the American Society of Nephrology/International Society of Nephrology World Congress of Nephrology, San Francisco, CA, October 15, 2001.

181E. Safety profile of lanthanum carbonate in hemodialysis patients: results from a phase III U.S. study. *Melanie S. Joy, Pharm.D.*, William F. Finn, M.D.; University of North Carolina, Chapel Hill, NC.

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182E. Results of a randomized, phase III, dose-titration, parallel group study of lanthanum carbonate for reduction and maintenance of serum phosphate in chronic hemodialysis patients. *Melanie S. Joy, Pharm.D.*, William F. Finn, M.D.; University of North Carolina, Chapel Hill, NC.

Published in J Am Soc Nephrol 2001;12:388A.

183. Evaluation of secondary complications and medication use in patients with early chronic kidney disease. *Roya M. Sameri, Pharm.D.*, Joanna Q. Hudson, Pharm.D., Kim Huch, M.D.; University of Tennessee, Memphis, TN.

PURPOSE: Complications of chronic kidney disease (CKD) arise early in the course of the disease and are associated with adverse outcomes. Guidelines for management of complications in ESRD patients (pts) are generally applied to the early CKD population due to the absence of standardized guidelines. Data from adult CKD pts not requiring dialysis were evaluated to 1) evaluate management of secondary complications; 2) determine medication (MED) prescribing patterns, and 3) identify potential areas for intervention.
METHODS: Select laboratory data, MED profiles, and demographic information were collected for pts in an outpatient nephrology clinic by chart review and patient interviews. This information was evaluated in the context of recommendations in CKD patients to determine overall management and areas for intervention.
RESULTS: CKD pts = 100; Demographics: 87% black, 61% female, mean age 50.9 ± 14 years; cause of CKD: HTN 62%, diabetes 26%. Lab data: Mean serum creatinine 3.0 ± 1.8 mg/dL, estimated creatinine clearance 48.2 ± 38.6 mL/min, Hct 33.4 ± 5.4%, phosphorus 3.9 ± 1.1 mg/dL, albumin 3.4 ± 0.64 g/dL. Mean systolic and diastolic BP were 136 ± 25 mm Hg and 81 ± 13 mm Hg, respectively. MED use: Diuretics 67%, CCB 50%, ACE inhibitors 41%, β-blockers 22%, ARB 3%, antidiabetic agents 34%, phosphate binders 18%, erythropoietin 3%, iron supplements 13%, median number of MEDs/patient = 5.

Guideline/Recommendation	Areas for Intervention
Anemia: HCT 33-36%	30% of pts with HCT < 30%
Alb < 3.5 g/dL associated with ↑ mortality	43% of pts with alb < 3.5 g/dL
BP <130/85 mm Hg, (<125/75 if >1g/day proteinuria)	59% of pts on ≥ 2 antihypertensive agents
ACE Inhibitors / ARBs for proteinuria	49% of pts with proteinuria not on ACE Inhibitor or ARB
Ca 9.2-9.6 mg/dL, Phos 2.5-5.5 mg/dL	All phosphate binders calcium-containing; No documented Vitamin D use

CONCLUSION: Pharmacist participation in the care of pts with CKD through protocol development and implementation may provide more rational MED use and improve management of secondary complications in early CKD.

Neurology

184. The use of herbal supplements and vitamins by patients with amyotrophic lateral sclerosis. *Orly Carter, Pharm.D.*, Mark B. Bromberg, M.D.; University of Utah Hospitals and Clinics; University of Utah, Salt Lake City, UT.

PURPOSE: Alternative medicine use is widespread in all industrialized western countries. Patients with chronic and incurable diseases are particularly inclined to seek alternative treatments, as documented by previous studies. Although other investigators addressed the use of alternative medicine by ALS patients, there are no published data regarding the use of botanical or herbal supplements in ALS. Our objective was to survey patients with ALS in our clinic regarding their use of vitamins, herbal supplements, and other compounds.
METHODS: Study subjects were followed by the University of Utah Motor Neuron Disease Clinic. A questionnaire was mailed to subjects and was designed to assess: 1) disease onset and duration; 2) use of riluzole, vitamins, herbal supplements, and other compounds; and 3) sources of information and expectations of products.
RESULTS: A total of 53 subjects participated; mean age 60 years old (range 39-83 years), 15 females, 38 males. Symptom duration averaged one to five years (45 limb onset, 8 bulbar onset). 32% were taking riluzole. 70% were taking vitamins, 42% were taking herbal supplements, and 21% were taking other compounds (prescription medications used for ALS, but not indicated for ALS). Information about herbal medicines was obtained mostly via friends and relatives (n=17), a physician (n=20), and the Internet (n=9). Our patients selected "improvement of general well being" and "slowing of disease progression" most often as reasons for using herbal supplements, vitamins, and other compounds.
CONCLUSIONS: Our study demonstrated that the majority of ALS study subjects take vitamins, herbal supplements, or unproven prescription drugs.

185E. Disposition of cefepime in the central nervous system in patients with external ventricular drains. *Denise H. Rhoney, Pharm.D.*, Vincent H. Tam, Pharm.D., Dennis Parker, Jr., Pharm.D., Peggy S. Mckinnon, Pharm.D., William M. Coplin, M.D.; Wayne State University, Detroit, MI.

Presented at the 54th Annual Meeting of the American Academy of Neurology, Denver, CO, April 17, 2002.

186. Nitroglycerin-induced headache in migraineurs: assessment by $H_2{}^{15}O$ PET. *Edward M. Bednarczyk, Pharm.D.*, Linda Hershey, M.D., Ph.D., David Wack, M.S., Jayakumari Gona, M.D.; University at Buffalo, Buffalo, NY

PURPOSE: Nitroglycerin (GTN) is widely known to induce headache and has been used as an experimental model of migraine headache in healthy volunteers. Relatively little is known about the effects of GTN on migraineurs. This study used PET to study the influence of GTN on global and regional cerebral blood flow (CBF, rCBF) in migraineurs.
METHODS: Subjects meeting IHS criteria for migraine with or without aura were studied. Subjects with significant neurologic, psychiatric, or other medical conditions were excluded. Neither prophylactic or analgesic medications were permitted at the time of study. CBF and rCBF was measured using $H_2{}^{15}O$ at baseline, following IV GTN infusion at 0.125, 0.25, and 0.5 µg/kg/min, and 30 and 60 minutes following discontinuation of GTN. rCBF was determined using the widely accepted approach of statistical parametric mapping (SPM).
RESULTS: Nine subjects have been scanned to date. CBF values (ml/min/100 g) are as follows.

	Baseline	GTN 0.125*	GTN 0.25*	GTN 0.5	30 min p GTN	60 min p GTN
Mean (SD)	49 (5)	59 (15)	57 (11)	54 (19)	55 (16)	49 (9)

*p<0.05 compared to baseline

Significant increases in rCBF were found in the meninges at 0.5 µg/kg/min GTN and persisted 30 and 60 minutes post GTN. Significant reductions in rCBF were identified in the left temporal and occipital lobes at 0.25 and 0.5 µg/min GTN. Occipital reductions in rCBF persisted 30 and 60 minutes post GTN.
CONCLUSIONS: In migraineurs, GTN induced expected increases in global CBF. GTN induces changes in rCBF that should be compared with spontaneous migraine headache.

187. Correlation of levetiracetam concentrations between serum and saliva. *Shellee A. Grim, Pharm.D.,* Melody Ryan, Pharm.D., BCPS, CGP, Michael V. Miles, Pharm.D., Peter H. Tang, Ph.D., Richard H. Strawsburg, M.D., Ton J. deGrauw, M.D., Ph.D., Robert J. Baumann, M.D.; University of Kentucky, Lexington, KY; Cincinnati Children's Hospital, Cincinnati, OH.

PURPOSE: More than 100 drugs have been evaluated for salivary TDM since the 1970s; phenytoin, phenobarbital, and carbamazepine have demonstrated tight correlations between serum and saliva concentrations. There are no published data for levetiracetam. The objective of this study was to determine the correlation between levetiracetam serum and saliva concentrations.
METHODS: Investigators identified outpatients who were taking levetiracetam and for whom a serum concentration was ordered by their physician. Saliva samples were obtained by spitting. Blood samples were obtained by phlebotomy. Serum and saliva levetiracetam concentrations were determined via HPLC. Regression analysis was utilized to determine correlations.
RESULTS: Serum and saliva samples were obtained from 36 patients (21 female, 15 male) whose ages ranged from 3-57 years (mean 25.4 ± 15.6). Three patients were given one drop of lemon juice to stimulate saliva production. Saliva to serum concentration ratio ranged from 0.10 to 0.95 (mean=0.427 ± 0.176). Regression analysis showed an r-value of 0.88.
CONCLUSION: We demonstrated a positive correlation between levetiracetam saliva and serum concentrations. Our data suggest that saliva monitoring can help the clinician to monitor levetiracetam therapy. We believe that saliva monitoring will facilitate sample collection and improve the quality of life for persons with epilepsy; especially individuals with poor venous access such as children and elderly patients and persons afraid of needles.

188. Correlation of lamotrigine concentrations between serum and saliva. *Melody Ryan, Pharm.D., BCPS, CGP,* Shellee A. Grim, Pharm.D., Michael V. Miles, Pharm.D., Peter H. Tang, Ph.D., Richard H. Strawsburg, M.D., Ton J. deGrauw, M.D., Ph.D., Robert J. Baumann, M.D.; University of Kentucky, Lexington, KY; Cincinnati Children's Hospital, Cincinnati, OH.

PURPOSE: More than 100 drugs have been evaluated for salivary TDM since the 1970s; phenytoin, phenobarbital, and carbamazepine have demonstrated tight correlations between serum and saliva concentrations. There are two published studies correlating serum and saliva concentrations of lamotrigine. However, neither study included individuals younger than 16 years. The objective of this study was to determine the correlation between lamotrigine serum and saliva concentrations for individuals of all ages.
METHODS: Investigators identified subjects at the University of Kentucky neurology clinic who were taking lamotrigine for whom a serum concentration was ordered. Saliva samples were obtained by spitting into a cup. Blood samples were obtained by phlebotomy. Serum and saliva lamotrigine concentrations were determined via HPLC and regression analysis was utilized to determine correlations.
RESULTS: Serum and saliva samples were obtained from 21 patients (12 female, 9 male). Ages of these patients ranged from 2-46 years (mean=20 ± 11 years). Saliva to serum concentration ratio ranged from 0.41 - 0.91 (mean=0.58 ± 0.12). Regression analysis showed an r-value of 0.97. For the five patients ≤ 12 years, the saliva to serum concentration ratio mean was 0.52 ± 0.12.
CONCLUSION: We demonstrated high correlation between saliva and serum concentrations for lamotrigine. The data suggest that saliva monitoring may play a role in the monitoring of lamotrigine for individuals of all ages. While saliva monitoring may facilitate sample collection and improve the quality of life for all patients with epilepsy; children, elderly patients, others with poor venous access, and those with fear of needles may benefit especially from this technology.

189E. A retrospective review of identifying and treating hyperlipidemia in stroke patients before and after American Heart Association recommendations. *Shana L. Lettieri, Pharm.D.,* Kady Flannery, Pharm.D., Robert Dombrowski, Pharm.D., Andrea South, B.S., Brett South, B.S.; Veterans Affairs Maryland Health Care System, Baltimore, MD.

Presented at the Eastern State Conference of Pharmacy Residents and Preceptors, Baltimore, MD, April 25, 2002.

190E. Evaluation of captopril for the management of hypertension in autonomic dysreflexia: a pilot study. Zahida Esmail, B.Sc.Pharm., *Karen F. Shalansky, Pharm.D., FCSHP,* Rubina Sunderji, Pharm.D., FCSHP, Hugh Anton, M.D., FRCP, Keith Chambers, M.D., M.H.Sc., William Fish, M.D.; Vancouver General Hospital; G.F. Strong Rehabilitation Hospital, Vancouver, BC, Canada.

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Nuclear Pharmacy

191E. Safety and efficacy of 213Bi-[DOTA^0,Tyr^3]octreotide (Bi-DOTATOC) in peptide receptor radionuclide therapy of neuroendocrine tumors in a pre-clinical model. *Jeffrey P. Norenberg, Pharm.D.,* Boudewijn J. Krenning, M.D., Inge R. Konings, M.D., Marion De Jong, Ph.D., Kayhan Garmestani, Ph.D., Martin W. Brechbeil, Ph.D., Donna F. Kusewitt, Ph.D., Larry K. Kvols, M.D.; University of New Mexico, Albuquerque, NM; Erasmus University Rotterdam, Rotterdam, Netherlands; National Cancer Institute, Bethesda, MD; Ohio State University, Columbus, OH; University of South Florida, Tampa, FL.

Presented at the 2001 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Miami, Fl, October 2001.

Nutrition

192. Assessment of hyperglycemia and associated complications in total parenteral nutrition patients. *Claire Avante, Pharm.D.,* John Siepler, Pharm.D., Jeff King, Pharm.D., John Inciardi, Pharm.D.; University of California Davis Medical Center, Sacramento, CA.

PURPOSE: Hyperglycemia is common in critically-ill patients and in total parenteral nutrition (TPN) patients. Intensive blood glucose control between 80 mg/dL and 110 mg/dL decreased mortality in septic patients with multi-organ dysfunction, and in intensive care unit (ICU) stays greater than 5 days. We evaluated hyperglycemia and associated complications in ICU patients on TPN with standard practice of glucose control.
METHODS: We performed a retrospective review of 99 ICU patients on TPN. Blood glucose control within the first 21 days was stratified into group I (< 110 mg/dL), group II (110-150 mg/dL), group III (150-180 mg/dL) or group IV (> 180 mg/dL). The outcomes were clinical diagnosis of infection, a septic picture, duration of ICU stay, and mortality.
RESULTS: Of 99 patients in the ICU (duration = 27.4 ± 23.8 days) on TPN (27.4 ± 3.03 kcal/kg) multi-variate analysis found no associations between high blood glucose and outcome measures. However, other variables including age (p=0.043), hepatic impairment (p=0.029) and a trend in diabetics (p=0.056) predicted clinical diagnosis of infection. Renal impairment (p=0.001) predicted sepsis. Renal impairment (p=0.03) and higher TPN kcal/kg (p=0.025) predicted prolonged ICU stay. Hepatic impairment (p=0.008), renal impairment (p=0.018), age (p=0.002), and higher TPN kcal/kg (p=0.027) predicted mortality.
CONCLUSION: Although intensive insulin therapy has shown to decrease mortality, these patients did not reveal the same benefits of tight glucose control. These findings are attributed to inadequate power in the euglycemic patient group and the evaluation of a different patient population. However, this study concurs with previous findings that age, pre-existing organ dysfunction, diabetes, and higher TPN kcal/kg are associated with increased complications.

193. The effect of orlistat on weight reduction in obese patients. *Jung M. Oh, Pharm.D.,* Soo M. Ahn, M.S.; Sookmyung Women's University, Seoul, Korea.

PURPOSE: The objective of this study was to evaluate the effects of orlistat on weight reduction and parameters associated with risk factors of cardiovascular or metabolic disorders and assess the factors affecting weight reduction in obese patients taking Orlistat.
METHODS: All adult obese patients (body mass index over 25 kg/m^2) who received orlistat for 24 weeks continuously at Asan Medical Center were retrospectively evaluated for the changes in weight, waist and hip circum-

ference, body fat, serum lipid profile, fasting glucose and blood pressure.
RESULTS: A total of 63 patients were included for the evaluation of changes in weight, waist and hip circumference, body fat, serum lipid profile, fasting glucose and blood pressure. After 24 weeks of treatment, mean reductions in weight, BMI and waist circumference from baseline were 3.6 ± 2.9 kg ($p<0.001$), 1.4 ± 1.1 kg/m^2 ($p<0.001$), and 4.4 ± 3.8 cm ($p<0.001$), respectively. Eight percent of patients lost the weight over 10% of their initial weight. The number of patients with high risk of metabolic disorders (male >102 cm, female >88 cm) decreased to 24 from 35 patients after 24 weeks of treatment. Body fat was also reduced by 2.9 ± 2.5% from baseline ($p<0.001$) after 24 weeks of treatment. The mean reductions in total cholesterol level and fasting blood glucose level from baseline were significant with 11.4% ($p=0.005$), and 14.1% ($p=0.029$), respectively. Mean systolic and diastolic blood pressure decreased from 132.0 ± 19.1 mmHg to 120.4 ± 14.6 mmHg ($p<0.001$), and 75.7 ± 11.8 mmHg to 71.7 ± 11.3 mmHg($p=0.014$), respectively. However, there were no significant changes in LDL cholesterol, triglyceride and HDL cholesterol levels. The side effects reported with the use of orlistat were mild gastrointestinal effects.
CONCLUSIONS: Orlistat was effective in reducing weight, abdominal fat distribution and body fat, and in improving parameters associated with risk factors of cardiovascular and metabolic disorders.

194E. Glutamine and bombesin do not regulate gut-associated lymphoid tissue via mucosal addressin cell adhesion molecule-1. *Gordon S. Sacks, Pharm.D.*, Shigeo Ikeda, M.D., Kenneth A. Kudsk, M.D., Cheryl D. Johnson, Ph.D., Ben L. Zarzaur, M.D.; University of Wisconsin, Madison, WI; University of Tennessee, Memphis, TN.

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195. Sterility of lipid emulsions following 24-hour infusion. *Catherine M. Crill, Pharm.D.*, Emily B. Hak, Pharm.D., Richard A. Helms, Pharm.D.; University of Tennessee Health Science Center; Le Bonheur Children's Medical Center, Memphis, TN.

PURPOSE: Based on studies that show lipid emulsion (LE) supports microbial growth in inoculated LE, the CDC Hospital Infection Control Practices Advisory Committee recommends that LE solutions be infused within 12 hours while total nutrient admixtures may be infused over 24 hours (based on no greater microbial growth than non-LE containing parenteral nutrition (PN) solutions). Studies have not evaluated microbial growth for LE spiked under sterile conditions and infused from bottle to patient over 24 hours.
METHODS: On 2 study days (separated by 8 weeks), LE (Intralipid 20%, Baxter) bottles were spiked under laminar flow conditions and hung at pediatric patients' bedsides to infuse with PN (via y-site) for 24 hours. The technician spiking and the nurses hanging the solutions had no prior knowledge of the experiment. After 24-hour infusion, 10 ml samples were withdrawn from LE bottles under aseptic conditions and refrigerated until the following morning. The hospital microbiology laboratory then inoculated the samples into blood culture bottles and incubated them (BacT/ALERT Incubator Module, Biomerieux) for 5 days. The samples were subcultured to blood agar plates with olive oil and incubated for 2 days (CO_2 incubator).
RESULTS: On each of the study days, 9 bottles were sampled (n=18). Nine of the bottles were from ICU patients. At 7 days, all 18 LE samples showed no bacterial or fungal growth (including Malassezia furfur).
CONCLUSIONS: The practice of spiking LE bottles under sterile conditions and hanging them (not repackaging) over a 24-hour period may not increase the risk for microbial contamination.

Oncology

196. Clinical and economic outcomes of a formulary change from filgrastim to sargramostim in patients receiving myelosuppressive chemotherapy. *Holly O. Chan, Pharm.D.*, Siu Fun Wong, Pharm.D.; University of California Irvine Medical Center, Irvine, CA; Western University of Health Sciences, Pomona, CA.

PURPOSE: Based on studies that suggest filgrastim (G-CSF) and sargramostim (GM-CSF) are therapeutically equivalent, the Pharmacy Department at UCI implemented a formulary change from G-CSF to GM-CSF. This study evaluates clinical and economic outcomes of this formulary change.
METHODS: A retrospective chart review was conducted in patients ≥ 18 years old with melanoma, lymphoma, breast, ovarian and lung malignancies who received ≥ 5 doses of G-CSF or GM-CSF as primary or secondary prophylaxis following conventional-dose myelosuppressive chemotherapy from Jan 1995 to March 2002. Patients treated before Jan 2000 received G-CSF whereas those treated after that date received GM-CSF. Clinical outcomes evaluated included time to ANC > 1500, incidence of febrile neutropenia, subsequent chemotherapy dose delay, and adverse events. Resource utilization data was collected.
RESULTS: Twenty-nine and 27 patients received G-CSF and GM-CSF, respectively. (priority 2 if number of words allowed - you may insert a sentence here to identify the number of pts with primary vs secondary prophylaxis). Time to ANC recovery in patients receiving G-CSF and GM-CSF was 16.7 days and 18.6 days (p = NS). One (3.4%) patient in G-CSF group developed febrile neutropenia, as compared with four (14.8%) in GM-CSF group. More patients treated with GM-CSF experienced dose delay (11 vs. 4, $p < 0.05$). Overall incidence of adverse events was similar, but more patients in the GM-CSF group had fever and fatigue. Patients treated with GM-CSF required more platelet and red blood cell transfusions, antibiotics, and hospitalizations.
CONCLUSION: The formulary change from G-CSF to GM-CSF was associated with a higher incidence of febrile neutropenia, subsequent chemotherapy dose delay, and greater resource utilization. These results suggest that G-CSF and GM-CSF are not therapeutically equivalent.

197. Topical doxepin 5% cream for chemotherapy-induced painful polyneuropathy. Brian L. Brice, M.D., *Rachel J. Clark-Vetri, Pharm.D.*; Fox-Chase Temple Cancer Center; Temple University, Philadelphia, PA.

PURPOSE: This is a pilot study investigating the safety and efficacy of topical doxepin as an adjuvant analgesic in the management of chemotherapy-induced painful polyneuropathy (CIPP).
METHODS: This is a randomized, double-blind, placebo controlled study of oncology patients with CIPP. Patients were randomized to use topical doxepin hydrochloride 5% cream (Bioglan) or placebo cream. The presence of NCI grade 2 CIPP was determined through physical examination and nerve conduction studies. The study cream or placebo was applied to affected areas three times a day. Pain was assessed using neuropathic pain scales at baseline and weekly for 4 weeks. Side effects and concomitant analgesic use were closely monitored.
RESULTS: Nine patients were recruited and eight were enrolled. All enrolled patients completed the 4-week study period. Paclitaxel was the causative agent in seven patients, vincristine for one patient. There were no statistically significant differences between the baseline group characteristics. Using mixed modal analysis of variance for repeated measures, a reduction in thermal dysesthesia was demonstrated for doxepin ($p<0.05$). There was a trend towards significance for reduction in pain intensity ($p=0.06$). No significant side effects were reported.
CONCLUSION: This pilot study suggests that topical doxepin is a safe and effective adjuvant treatment for CIPP. This result is consistent with current use of systemic tricyclic antidepressants for similar conditions. A larger study would help determine appropriate dosing, duration of therapy and magnitude of analgesic effect.

198E. Factors associated with early termination of CHOP, and its association with overall survival among patients with intermediate-grade non-Hodgkin's lymphoma. Elizabeth Chrischilles, Ph.D., Brian Link, M.D., *Shane Scott, Pharm.D.*, David J. Delgado, Ph.D., Moshe Fridman, Ph.D.; University of Iowa, Iowa City, IA; Amgen, Thousand Oaks, CA; AMF Consulting, Los Angeles, CA.

Presented at the 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 18-21, 2002.

199E. Liposome-encapsulated *c-raf* antisense oligodeoxynucleotide in patients with advances solid tumors: phase I study of daily infusion during radiation therapy. *Anatoly Dritschilo*, Chao H. Huang, Lewis C. Strauss, Christina K. Fleming, Aquilur Rahman, Charles Rudin, Brian Collins, John Marshall, Anu Singh, Chuanbo Zhang, Deepak Kumar, Prafulla Gokhale, Usha N. Kasid; Georgetown University Medical Center, Washington, D.C.; Temple University, Philadelphia, PA; NeoPharm Inc, Lake Forest, IL; University of Chicago, Chicago, IL.

Presented at the 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 18-21, 2002.

200E. Pegfilgrastim was observed to be as safe and effective as filgrastim in elderly patients with breast cancer. Jeffrey E. Shogan, M.D., Heinz Koelbl, M.D., Frankie Ann Holmes, M.D., *Sally Yowell, Pharm.D.*, et al.; University of Pittsburgh Medical Center, Pittsburgh, PA; Universitatsklinikum Halle, Halle Germany; U.S. Oncology, Houston, TX; Amgen, Inc., Thousand Oaks, CA; Duke University Medical Center, Durham, NC.

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201. Reducing anti-DT IgG concentrations to improve the efficacy of a diphtheria fusion protein. *Philip D. Hall, Pharm.D.*, Arthur E. Frankel, M.D.; Medical University of South Carolina, Charleston, SC; Wake Forest University, Winston-Salem, NC.

PURPOSE: Because of the poor survival in acute myeloid leukemia (AML), we are developing a novel fusion protein consisting of a truncated diphtheria toxin linked to human granulocyte macrophage colony stimulating factor (DT_{388}GMCSF). Pre-existing anti-DT IgG can bind and remove DT_{388}GMCSF from the circulation. In our phase I trial of DT_{388}GMCSF in relapsed or refractory AML, patients with high concentrations of pre-existing anti-DT IgG (> 2 µg/mL) had significantly lower DT_{388}GMCSF concentrations (Clin Cancer Res 2002;8:1004-13). One method to lower pre-existing anti-DT IgG

concentrations would be to bind the anti-DT IgG with DT_{388}GMCSF. To determine the feasibility of this hypothesis, we retrospectively measured anti-DT IgG concentrations before treatment and after four days of treatment with DT_{388}GMCSF.
METHODS: Patients (n=23) with relapsed or refractory AML in the phase I trial received DT_{388}GMCSF at doses from 1-5 µg/kg/day intravenously for five days. Patients (n=4) on the phase II study received 4 µg/kg/day for 5 days. Serum anti-DT IgG concentrations pre-treatment and after four days of treatment were measured by an enzimoimmunoassay (Clin Immunol 2001;100:191-7).
RESULTS: The median anti-DT IgG concentration pre-therapy was 2.4 µg/mL (range: undetectable - 9.4) and significantly decreased to a median concentration of 1 µg/mL after four days of treatment with DT_{388}GMCSF ($p = 0.0001$). Twenty-four of the 27 (89%) patients had a decrease in their anti-DT IgG concentrations. Importantly, nine of 11 patients with pre-therapy anti-DT IgG concentrations > 2 µg/mL had a decrease to ≤ 1.6 µg/mL. The median fold change in anti-DT IgG concentrations was 3.8 (range: 0.5-12.5). There was no relationship between dose of DT_{388}GMCSF with the absolute change or fold change in anti-DT IgG concentrations.
CONCLUSION: Treatment with four days of DT_{388}GMCSF significantly lowered anti-DT IgG concentrations and may increase the patients' exposure to subsequent doses of DT_{388}GMCSF. Based on these results, we intend to compare the pharmacokinetics from day 1 and day 5 of treatment in patients on the phase II trial.

202. Carboplatin dosing adult cancer patients: a survey of oncology pharmacy practitioners in the United States. *Robert J. Ignoffo Pharm.D.*, Masha Lam, Pharm.D.; University of California, San Francisco, CA.

PURPOSE: 1) evaluate practice patterns of oncologists in the US that prescribe carboplatin; 2) assess the impact of patient weight and serum creatinine (Cr) in the dosing of carboplatin.
METHODS: 1290 surveys were e-mailed to a random selection of medical or gynecologic oncologist members of the American Society of Clinical Oncology. Two-hundred and forty surveys were sent to oncology pharmacist members of the American College of Clinical Pharmacy. The survey contained 14 multiple choice questions in the following categories: demographics (4); frequency of carboplatin use (1); formulae used in dosing carboplatin (2); impact of low serum Cr or high estimated Cr clearance on prescribers' decision in carboplatin dosing (4); and the impact of patient weight (obesity) in carboplatin dosing (3).
RESULTS: 75 responses were obtained; 12 from oncologists (1.2%) and 62 (24.5%) from oncology pharmacists. Eighty percent of respondents had been practicing 3 years or longer. Sixty-three percent practiced hospital-based, academic practice. Sixty-five percent of the group reviewed orders in 10 or more patients a month. The Calvert Formula was used by 92% of responders. Seventy-eight percent considered low creatinines to be 0.7 mg/dl or lower, which were either adjusted to 1 mg/dl or creatinine clearances capped at 180 ml/min. Most responding practitioners considered obese patients to 120 to 140% above their ideal body weight. Sixty-two percent would adjust the carboplatin dose for an 'obese' patient but a variety of weights were chosen for the adjustment.
CONCLUSION: Practitioners use several methods of dosing carboplatin despite a published method of dosing.

203. Dose intensity of oxaliplatin in 5-fluorouracil and leucovorin regimens in pretreated metastatic colorectal cancer. Kyong J. Jeong, M.S., Jung M. Oh, Pharm.D., Seung K. Choi, Ph.D., Doyeun Oh, M.D., Ph.D.; Sookmyung Women's University, Seoul, Korea; Pochon CHA University, Kyonggi-do, Korea.

PURPOSE: Previous studies of oxaliplatin, 5-fluorouracil and leucovorin combination therapy in pretreated metastatic colorectal cancer showed that oxaliplatin dose intensity is an important prognostic factor for objective response rates and progression free survival. This study was designed to evaluate the response rates, progression free survival and toxicities of oxaliplatin, 5-fluorouracil and leucovorin combination regimen according to oxaliplatin dose intensity in pretreated metastatic colorectal cancer.
METHODS: Data were retrospectively collected from medical charts of patients treated with oxaliplatin, 5-fluorouracil and leucovorin combination regimen in two university medical centers between May 2000 and October 2001. Oxaliplatin dose intensity over a two-week period was calculated for those patients who received at least five consecutive cycles of the combination regimen. Of the 63 patients evaluated, 42 patients received low dose intensity (≤ 85 mg/m^2/2 weeks) oxaliplatin while 21 patients received high dose intensity (> 85 mg/m^2/2 weeks) oxaliplatin. Responses to combination regimen were evaluated on the fifth cycle of chemotherapy according to WHO definitions of objective response and toxicities were measured every cycle of chemotherapy according to NCI-CTC criteria.
RESULTS: Objective responses occurred in 10 (47.7%) patients receiving high dose intensity and in 9 (21.4%) patients receiving low dose intensity ($p=0.014$). Median progression free survivals were 24.7 weeks in high dose intensity group and 20.5 weeks in low dose intensity group ($p=0.344$). Forty-five percent of high dose intensity group and 33.5% of low dose intensity group experienced progression free at 6 month. However, oxaliplatin dose intensity was not associated with neutropenia, thrombocytopenia, neuropathy nor nausea and vomiting.
CONCLUSIONS: The study showed that oxaliplatin dose intensification significantly improves the objective response rate in pretreated metastatic colorectal cancer without causing severe toxicity.

204E. Darbepoetin alfa effectively alleviates anemia in patients with chronic anemia of cancer: efficacy and pharmacokinetic results. *Dora Liang, Pharm.D.*, Robert Smith, M.D., Greg Rossi, Ph.D., Alan Colowick, M.D.; University of California at Los Angeles, Los Angeles CA; SC Oncology Associates, Columbia; Amgen Inc, Thousand Oaks, CA.

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205E. Optimizing the management of anemia in cancer patients: a randomized, active-controlled, study investigating the dosing of darbepoetin alfa. *Dora Liang, Pharm.D.*, John Glaspy, M.D., Greg Rossi, Ph.D., Alan Colowick, M.D.; University of California at Los Angeles, Los Angeles CA; Amgen Inc, Thousand Oaks, CA.

Published in Proc Am Soc Clin Oncol 2002;21:362a.

206E. Unconditional and conditional risk models can be used to predict neutropenic complications associated with breast cancer adjuvant therapy. *Olayemi Agboola*, Jeffrey Crawford, M.D., David Dale, M.D., Haim Erder, Moshe Fridman, August Salvado, M.D., Carol Brannon, Gary H. Lyman, M.D.; ANC Coordinating Center, Albany, NY; Duke University, Durham, NC; University of Washington, Seattle, WA; Amgen, Thousand Oaks, CA; University of Rochester Medical Center, Rochester, NY.

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207. Increased chemotherapy dose attenuation in elderly patients: evidence from surveys of practice patterns in early-stage breast cancer and non-Hodgkin's lymphoma. Lodovico Balducci, M.D., Andrew D. Zelenetz, M.D., *Gary H. Lyman, M.D.*; University of South Florida, Tampa, FL; Memorial Sloan-Kettering Cancer Center, New York City, NY; University of Rochester Medical Center, Rochester, NY.

PURPOSE: Otherwise healthy elderly cancer patients can achieve outcomes equal to younger patients if given equal therapy and appropriate supportive care; however, general belief is that elderly patients benefit less from chemotherapy and suffer more toxicity. Data from two large nationwide surveys of practice patterns of early-stage breast cancer (ESBC) and non-Hodgkin's lymphoma (NHL) treatment were analyzed to determine the prevalence of undertreatment of elderly patients.
METHODS: The ESBC database contains 20,799 patient records from 1243 community practices (96% received CMF, CAF, or AC). The NHL database contains records for 3165 patients with newly diagnosed intermediate-grade NHL (100% CHOP, CNOP, or CVP) from 405 practices. The primary endpoint was low planned dose on time (LPDOT), defined as < 85% for ESBC and < 80% for NHL.
RESULTS: Among ESBC patients, 16.5% were ≥ 65 years; 57.4% of elderly patients received CMF versus 43.6% overall. Older patients were more likely to receive LPDOT for CMF (27.8% vs. 20.6%*), CAF (29.1% vs. 12%*) and AC (14.7% vs. 10.2%*) than their younger counterparts. Among NHL patients, 49% were ≥ 65 years; compared to younger patients, they were less likely to receive CHOP (76% vs. 89%*) and more likely to have planned (27% vs. 12%*) and received (42% vs. 23%*) LPDOT. Dose reductions were more common than primary G-CSF prophylaxis, and G-CSF use was often suboptimal (*$p<0.001$).
CONCLUSION: In community practice, elderly patients with ESBC and NHL frequently receive less aggressive chemotherapy than younger patients. Recognition and appropriate G-CSF use could improve outcomes for these patients.

208E. Delivered dose intensity in randomized clinical trials of chemotherapy for early-stage breast cancer and non-Hodgkin's lymphoma: better reporting is needed. David C. Dale, M.D., *Gordon McCarter, Ph.D.*, Jeffrey Crawford, M.D., Gary H. Lyman, M.D.; University of Washington, Seattle, WA; University of California, San Francisco, CA; Duke University, Durham, NC; University of Rochester Medical Center, Rochester, NY.

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209. Time to absolute neutrophil count recovery following filgrastim in patients with breast cancer. *Luis Meza, M.D.*, James Hackett, Ph.D., Theresa Neumann, Ph.D.; Southwest Oncology Associates, Lafayette, LA; Amgen Inc., Thousand Oaks, CA.

BACKGROUND: Filgrastim (Neupogen®) reduces the risk of chemotherapy-induced neutropenic complications and enables delivery of planned doses of chemotherapy on time by reducing the duration of severe neutropenia and decreasing the time to achieve ANC recovery.
METHODS: A retrospective analysis was performed examining the time to ANC recovery and the number of Filgrastim injections administered. Data

were analyzed from 222 patients with stage II-IV breast cancer receiving 4 cycles of doxorubicin 60 mg/m^2 plus docetaxel 75 mg/m^2 every 3 weeks in two phase 3 studies. Daily subcutaneous Filgrastim 5 µg/kg was administered per approved labeling; that is, beginning on day 2 of each chemotherapy cycle (approximately 24 hours after chemotherapy) and continuing until an ANC ≥ 10 x10^9/L after the expected ANC nadir was documented or for up to 14 days, whichever occurred first.
RESULTS: For each of the 4 cycles, a mean of approximately 11 daily Filgrastim injections were administered. As expected with an ANC dosing target of ≥ 10 x10^9/L, the median time to ANC ≥ 10 x10^9/L was also 11 days. Moreover, the median time to ANC recovery to ≥ 2 x10^9/L occurred at day 9 to 10 in cycles 1 through 4 (table).

Cycle	Median (Q1, Q3) Time to ANC ≥ 10 x10^9/L	Mean (SD) Number of Injections
1	11 (10, 12)	10.8 (1.9)
2	11 (10, 11)	10.5 (1.9)
3	11 (10, 12)	10.4 (1.9)
4	11 (10, 12)	10.5 (1.8)

[1]Kaplan-Meier median, Q1=25th percentile, and Q3=75th percentile

CONCLUSION: Across all cycles the average number of Filgrastim injections was approximately 11, consistent with median time to ANC ≥ 10 x10^9/L, while the median time ANC ≥ 2 x10^9/L was only 1 to 2 days fewer.

210. Clinical effects of the combination chemotherapy of heptaplatin and 5-fluorouracil in advanced gastric cancer. *Jung M. Oh, Pharm.D.,* Shin Gashil, M.S.; Sookmyung Women's University, Seoul, Korea.

PURPOSE: Heptaplatin is a platinum derivative with antitumor activity against gastric cancer. Preclinical studies showed that it is less toxic than other platinum analogs. The purpose of this study was to evaluate the efficacy and toxicity of the combination therapy of heptaplatin and 5-fluorouracil in advanced gastric cancer patients.
METHODS: This study retrospectively investigated 65 patients who had received at least 3 cycles of combination chemotherapy for unresectable advanced gastric cancer or with gastrectomy. No patients with prior radiotherapy was allowed. Patients received heptaplatin 400 mg/m^2 on Day 1 and 5-FU 1000 mg/m^2 on Day 1 ~ Day 5. The sequent doses were adjusted according to the toxicity and courses were repeated every 28 days. The clinical objective response was evaluated using CT scan after third cycles of combination chemotherapy and hematological and nonhematological toxicity were evaluated before and after each cycle.
RESULTS: The objective response occurred in 16 patients (24.6%). Two were complete and 14 were partial responses. Median progression free survival was 32 weeks with 29% of patients progression free at 1 year. The most common hematologic toxicity was anemia. Grade 3 or 4 anemia was seen in 2.7% of treatment cycles. Greater than grade 3 leucopenia were seen in 1.2% of cycles. Grade 3 or 4 neutropenia and thrombocytopenia occurred in 6.1% and 1.5% of cycles, respectively. The most common nonhematologic toxicity was proteinuria. Proteinuria was considerable factor for this chemotherapy although no patients experienced grade 3 or 4 proteinuria. Greater than grade 3 gastrointestinal toxicities were nausea and vomiting and diarrhea occurring in 4.6% and 1.5% of patients, respectively. Renal toxicity of Grade 2 with the elevation of serum creatinine was noted in 0.3% of cycles.
CONCLUSIONS: This study shows that combination therapy of heptaplatin and 5-FU has modest antitumor activity against advanced gastric cancer and renal toxicity that is regarded less toxic than that of other platinum analogues.

Pediatrics

211. Bowel frequency in critically ill children. *Karen D. Dominguez, Pharm.D.,* Matthew Borrego, Ph.D., Denise M. Coleman, M.D., Mark R. Crowley, M.D., Robert Katz, M.D.; University of New Mexico Health Sciences Center, Albuquerque, NM.

PURPOSE: The diagnosis of constipation in critically ill children is challenging since there is no clear definition. The purpose of this exploratory study is to determine if critical illness decreases stool frequency in children and to identify those risk factors that may affect stool frequency.
METHODS: All patients admitted to the PICU for more that 48 hours were eligible. Patients with any gastrointestinal disease known to alter stool output were excluded. The number of daily bowel movements for each patient was collected for the duration of the PICU stay. The patients' average number of daily bowel movements while in the PICU was compared to the patients' average number of daily bowel movements prior to illness, as reported by a parent, using a paired t-test. Predictors of stool frequency were determined by stepwise linear regression.
RESULTS: Fifty-eight patients were enrolled in the study. There was a statistically significant decrease in the number of daily bowel movements during critical illness (2.0 ± 1.1 vs. 0.6 ± 0.8, mean difference -1.4, CI 1.1-1.8). The variables that best predicted a decrease in bowel movements were male gender, length of PICU stay, the use of narcotics and the presence of hypercalcemia at any time during PICU admission (r^2 = 0.309).
CONCLUSION: Stool output is significantly reduced during critical illness and several factors affect stool output. This preliminary study will assist with the definition of constipation at our institution and the identification of children who may require prophylaxis.

212. Treatment of non-insulin dependent diabetes mellitus in pediatric patients. *Sandra Benavides, Pharm.D.,* Jeffrey Striet, John Germak, M.D., Milap C. Nahata, Pharm.D.; Ohio State University; The Children's Hospital, Columbus, OH.

PURPOSE: The purpose of the study was to determine efficacy of medications in the treatment of pediatric non-insulin dependent diabetes mellitus (NIDDM).
METHODS: All pediatric patients diagnosed with NIDDM from January 1996 to December 2001 were included in this retrospective study. Basic demographic information, presenting signs and symptoms, medication history and laboratory values were collected. The primary endpoints of the study were resolution of nocturia, polydipsia, and reduction of glycosylated hemoglobin (HbA_{1C}). Descriptive statistics and paired two-tailed t-tests using SPSS were used in the analysis.
RESULTS: A total of 45 patients, 18(40%) males and 27 (60%) females, were included in the study. The average age at diagnosis was 14.6 (SD ± 2.0) years. The signs and symptoms most commonly included polydipsia (79%), polyuria (69%), fatigue (35%) and concomitant infection (31%). Initial HbA_{1c} was 11 (SD ± 2.3). Patients treated with metformin (29%), sulfonylureas (18%), insulin (22%) or combination therapy (30%) did not have a significant decrease in HbA_{1c}. While receiving therapy, 50% of all patients still had symptoms defined as polydipsia, nocturia or glycosuria. Although 56% of patients had a decrease in HbA_{1c} from baseline after drug therapy, only 13% reached an HbA_{1c} < 6 %. Forty-one percent of the patients were non-compliant with therapy.
CONCLUSIONS: Pediatric patients with NIDDM have clinical features similar to adult patients. Monotherapy or combination therapy did not appear to significantly reduce HbA_{1c}. One possible explanation for the results could be the noncompliance with medications.

213E. Urinary free cortisol concentration in healthy and mild asthmatic children. *Hengameh H. Raissy, Pharm.D.,* Shawn M. Welch, Pharm.D., Patricia Marshik, Pharm.D., Susan Scott, M.D., H. William Kelly, Pharm.D.; University of New Mexico Health Sciences Center, Albuquerque, NM.

Presented at the International Conference of the American Thoracic Society, Atlanta, GA, May 19-22, 2002.

214. Pharmacists impact on caregivers of pediatric Latino patients with seizures in a neurology clinic. Maria Lopez, Pharm.D., *Kimberly Tallian, Pharm.D.,* William Lewis, M.D., David Haller, Pharm.D.; Children's Hospital, San Diego, CA.

PURPOSE: Medical education programs targeting underserved ethnic groups are needed to improve patient care and ultimately decrease medication-related hospital admissions. In 1992, the California State Council on Developmental Disabilities Statewide Epilepsy Report on the Needs Assessment for Multicultural Issues stated that there were several misconceptions about their disease, its treatment, and what to do during a seizure.
METHODS: We designed a study to evaluate the Latino caregiver's knowledge at baseline and following a comprehensive educational program provided by a pharmacist regarding their child's anticonvulsant medications with respect to dose, adverse effects, and storage. Caregivers were also surveyed at baseline and post education regarding their satisfaction with the information provided by all healthcare professionals as well as the amount of information the caregiver knew about proper seizure first aid and precautions. All new and return Latino caregivers of seizure patients were included in the study.
RESULTS: Thirty Latino caregiver's knowledge improved following the educational program provided by the pharmacists. Knowledge of anticonvulsant adverse effects, adverse event management, seizure first aid, medication storage, and seizure precaution for pre versus post pharmacist consultation improved from 0.16 to 0.93 ($p<0.05$), 0.47 to 0.97 ($p<0.05$), 0.33 to 1.0 ($p<0.05$), 0.30 to 1.0 ($p<0.05$), and 0.27 to 1.0 ($p<0.05$), respectively. All caregivers were also highly satisfied with the role of the pharmacist (0.36 to 0.93 ($p<0.05$)).
CONCLUSIONS: The pharmacist is perceived by the Latino caregiver to be a valuable medication education resource. Pharmacists can play an important role in the multidisciplinary approach to the management of pediatric patients with seizures.

215. The use of low dose Activase® for catheter clearance in pediatric patients. *May Saba, Pharm.D., BCNSP,* Judith Christie, R.N., MSN, Paul Munzenberger, Pharm.D.; Children's Hospital of Michigan; Wayne State University, Detroit, MI.

PURPOSE: This study evaluated the effect of a 1 mg dose of Activase® (Alteplase, TPA) for clearance of central venous catheters in pediatric patients.

METHODS: The number of patients reviewed was 111. The average patient age was 8.13 years (2 months-18 years). The central catheters studied included 88 Peripherally Inserted Central Catheters (PICC) with the average catheter size being 4 Fr (1.9 - 5Fr), 18 Broviac and short term central venous catheters (CVC) and 5 other central venous access: 1 Groshong catheter, 2 internal jugulars, and 2 ports. The fill volume of the different catheter sizes were < 1 ml. The average TPA dose administered was 0.9 mg (0.1-1 mg), with an average dwell time of 59 minutes (20-240 minutes).
RESULTS: With the use of 1 mg TPA dose, there were 91 out of 111 catheters that cleared (82%); 76 cleared after one dose of TPA (68%), 15 catheters cleared after a repeat dose of TPA (14%). 20 catheters failed to clear (18%); 10 catheters failed to clear after the first dose with no repeat dose given (50%) and 10 catheters failed to clear after a second dose was given (50%).
CONCLUSIONS: The fill volume of the catheters used in pediatric patients is less than 1 ml. The use of a 1 mg TPA dose for catheter clearance with a repeat of a 1 mg dose, as needed, may be sufficient in most pediatric patients.

216E. Effect of lansoprazole in intraesophageal pH in children with pathologic acid reflux. Linda Book, M.D., *Yi-Lin Chiu, Ph.D.,* Betsy Pilmer, BSN, David Gremse, M.D.; Primary Children's Medical Center, Salt Lake City, UT; Abbott Laboratories, Abbott Park, IL; TAP Pharmaceutical Products Inc., Lake Forest, IL; University of South Alabama, Mobile, AL.

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217. Pharmacokinetics of oral pantoprazole in pediatric patients. *Geraldine M. Ferron, Pharm.D., Ph.D.,* Laura P. James, M.D., Gregory L. Kearns, Pharm.D., FCCP, Jeffrey Blumer, M.D., Ph.D., Madelyn Abell, R.N., BSN, Barbara Mako, B.A., Philip R. Mayer, Ph.D., John Getsy, DMD, D.O., Jeffrey Paul, Ph.D.; Wyeth Research, Collegeville, PA; Arkansas Children's Hospital, Little Rock, AR; University of Arkansas for Medical Sciences, Little Rock, AR; Children's Mercy Hospital, Kansas City, MO; Rainbow Babies & Children's Hospital, Cleveland, OH.

PURPOSE: To evaluate the pharmacokinetics, tolerability, and safety of a single oral dose of pantoprazole in pediatric patients.
METHODS: Twenty-four (24) physiologically normal children, stratified by age (5-10 years, n=12; 11-16 years, n=12), who required acid suppression therapy any time during the 12 months preceding the study were randomly assigned to receive a single 20- or 40-mg pantoprazole enteric-coated tablet while fasting. Seventeen (17) patients had a previous history of dyspepsia; other gastrointestinal symptoms included gastritis (n=3), reflux (n=2), spastic colon (n=1), and gastric ulcer (n=1). Repeated venous blood samples were collected over 12 hours after drug administration. Plasma pantoprazole concentrations were measured by a HPLC/UV method and analyzed by non-compartmental methods. Pharmacokinetics were compared between age and dose groups and to adult data. Safety was monitored throughout the study.
RESULTS: Pharmacokinetic data from 3 children suggested the presence of slow metabolizer (elimination half-life > 3.5 hours) phenotype for CYP2C19. Data from the remaining subjects demonstrated dose proportionality and similarity between the two age groups. Mean pharmacokinetic data (maximum concentration of 3.8 mg/L for a 40 mg dose at 2.5 hours, terminal half-life of 0.63 h and clearance of 0.298 L/hour/kg) were similar to data obtained in adults. No significant association was observed between AUC, clearance and half-life and age. Pantoprazole was well-tolerated. There was only one mild non-drug related adverse event.
CONCLUSION: Pantoprazole pharmacokinetics in patients aged 5-16 years are similar to those in healthy adults. The pantoprazole dose for these patients may be the same as that for adults.

218. The impact of pharmacists' interventions on the discharge medication process: a randomized controlled trial. *Pierre Voirol, Ph.D.,* Sharon L. Youmans, Pharm.D., Chi Y. Chang, Pharm.D., Q. Laura Zhang, Pharm.D., Ceaminia S. Yuen, Pharm.D., Steven R. Kayser, Pharm.D.; University of California San Francisco; University of California San Francisco Medical Center, San Francisco, CA.

PURPOSE: This study evaluated the impact of clinical pharmacists' interventions during the discharge medication process on 1) patients and their caregivers' ability to obtain discharge medications in a timely fashion and 2) caregivers' knowledge of how to administer the medications as intended.
METHODS: Patients admitted to the pediatric ward from April 2, 2001 to March 29, 2002 were screened for inclusion into the study. Patients who met inclusion criteria and whose parent or legal guardian gave written informed consent were randomized to an intervention or control group. All interventions performed by pharmacy team members were documented. After patients were discharged to home, a structured phone interview was conducted with caregivers.
RESULTS: A total of 3278 patients were screened of whom 146 were randomized to the control group and 145 to the intervention group. More patients in the intervention group were able to obtain medications within 24 hours compared to the control group (84% vs. 69%, p=0.027). There was no statistical difference in the caregiver's knowledge of how to give the medications between the two groups.
CONCLUSION: Our results suggest that the coordinated efforts of pharmacists' interventions during the discharge process have a positive impact on patients' outcomes. These results can be used to formalize a discharge medication service and set criteria for patients at risk for having problems with obtaining medications at discharge.

219. Drug shortages in pediatrics. *Victoria Tutag Lehr, Pharm.D.,* Robert Franczak, R.Ph., Paul J. Munzenberger, Pharm.D., Michael Porvaznick, J.V. Aranda, M.D., Ph.D.; Wayne State University; Children's Hospital of Michigan, Detroit, MI.

PURPOSE: To identify cause and alternatives for recent drug shortages at Children's Hospital of Michigan.
METHODS: Pharmacy purchasing records (April 2000-November 2001) were reviewed to identify drugs listed as unavailable. Dosage form(s) and strength of drug, cause and projected duration of shortage were documented.
RESULTS: During this period, 43 drug products became unavailable or limited in supply. Anti-infectives (ciprofloxacin injection, gentamicin injection, penicillin injection, tobramycin powder, fluconazole injection, caspofungin injection, ganciclovir injection, bacitracin injection) were most frequent (18.6%;8/43), followed by vaccines/immunizations (pneumococcal conjugate, tetanus/diphtheria toxoids, influenza, hepatitis B), (9.3%;4/43) and opioids (fentanyl injection, meperidine injection, codeine liquid, Vicodin ES® tablets). Others were barbiturates (secobarbital oral, phenobarbital injection, pentobarbital injection), 7%; 3/43), vasoconstrictors (norepinephrine injection and phenylpropanolamine), (2/43; 4.7%), hematologic agents (preservative free heparin and urokinase), (2/43; 4.7%), and gastrointestinal agents (ranitidine liquid, cisapride), (2/43; 4.7%). L-asparaginase injection, prochlorperazine injection, diphenhydramine injection, magnesium sulfate injection, pyridoxine injection, and thiamine injection were also affected. Most shortages related to manufacturer production; (voluntary recalls mergers, diverting resources to other products, financial decisions, or increased market demands), (34/43); 79.1%, followed by product discontinuation (4/43); 9.3% and raw materials shortages (3/43); 7%. FDA safety recalls accounted for 2 of the drug shortages. Therapeutic alternatives were identified for 35.5% of the agents. Other measures included extemporaneous compounding and criteria based use.
CONCLUSIONS: Drug shortages occur frequently. Anti-infectives, vaccines/immunizations and opioids were most affected. Systems are needed to anticipate, and prevent drug shortages, and identify therapeutic alternatives.

220. The effect of combined use of inhaled and intranasal fluticasone propionate on the hypothalamic-pituitary-adrenal axis in children. *Glenn J. Whelan, Pharm.D.,* John J. Lima, Pharm.D., Dale Schrum, M.D., David Schaeffer, M.D., Floyd Livingston, M.D., Kathryn Blake, Pharm.D.; Nemours Children's Clinic, Jacksonville, FL; Nemours Children's Clinic, Orlando, FL.

Inhaled corticosteroids can suppress the hypothalamic pituitary adrenal (HPA) axis resulting in adrenal insufficiency. The objective of this study was to determine the additive effect of the combination of low dose inhaled fluticasone (Flovent®) and regular dose intranasal fluticasone (Flonase®) on HPA axis suppression and fluticasone exposure in children. There are no published data that evaluate the effect of combined low dose Flovent plus regular dose Flonase on the HPA axis in asthmatic children with allergic rhinitis.
This was a randomized, double blind, parallel, placebo controlled study. 27 asthmatic children with allergic rhinitis (4-12 years old) currently taking Flovent (88-100 µg/day), completed one month of baseline treatment with Flovent Diskus 100 µg/day, followed by randomization to treatment with Flovent Diskus 100 µg/day plus Flonase 100 µg/day or to Flovent Diskus 100 µg/day plus placebo for 28 days. HPA axis suppression was assessed by 12-hour (overnight) creatinine-corrected urine cortisol excretion (C_{Ux}), which was quantified by HPLC and tandem mass spectrometry. The 12-hour C_{Ux} was collected at the baseline and at the end of the treatment. Fluticasone exposure was assessed by quantifying serum concentrations of fluticasone by HPLC-MS at the end of treatment.
RESULTS:

	Placebo Group	Flonase Group	p-value
Baseline 12-hour C_{Ux} ± SD (mg cortisol/gm creatinine)	27.6 ± 21.6	27.3 ± 13.3	0.96
Day 28 12-hour C_{Ux} ± SD (mg cortisol/gm creatinine)	19.3 ± 20.1	22.1 ± 17.9	0.91
Serum fluticasone ± SD (pg/mL)	6.6 ± 6.8	17.8 ± 19.6	0.05

CONCLUSION: Addition of regular dose Flonase to low dose Flovent does not result in HPA axis suppression, despite increased fluticasone exposure.

221. The impact of education program on pediatric drug formulations. *You-Meei Lin, M.S.,* Tzu-Han Wu, M.S., Hui-Ping Liu, B.S., Yu-Hsuan Yen, M.S., Kuang-Yang Hsu, Ph.D., Hsiang-Yin Chen, M.S., Pharm.D.; Taipei Municipal Wan-Fang Hospital; Taipei Medical University, Taipei, Taiwan.

PURPOSE: Compounding extemporaneous powder formulation for pediatric patients is a common practice in Taiwan. The parents' demand that is believed to be unchangeable is one of the major factors influencing prescribing

patterns. The purpose of the study was to provide an educational program to intervene the parents' attitudes and knowledge regarding to extemporaneous formulation versus commercial solution product.
METHODS: Parents of pediatric patients admitted to Taipei Municipal Wan-Fang Hospital (TMWFH) were enrolled. The parents were divided into two groups according to the age of their children. A pharmacist provided an education program to introduce the compounding process and storage method of extemporaneous powder formulations to the parents individually. The advantages and disadvantages of the compounded powder and commercial product were also presented objectively. The scores from a questionnaire included 10 attitude questions in a 5-point scale and 10 knowledge questions in a dichotomous scale was compared before and after the program.
RESULTS: One hundred and two parents were recruited from March to April 2002 in TMWFH. After the education program, the total attitude scores of two groups were significantly improved from 30.0 to 36.5 and 30.0 to 36.0, respectively ($p<0.001$). The total knowledge scores of two groups were significantly increased from 4 to 9 and 5 to 9, respectively, after the education program ($p<0.001$).
CONCLUSION: The education program conducted by the pharmacist was associated with a change in attitudes and knowledge toward pediatric drug formulations. The change might provide further insight into behavioral adjustment.

222. Dolasetron for the prevention of postoperative vomiting in children undergoing strabismus surgery. *Deborah S. Wagner, Pharm.D.,* Uma Pandit, M.D., Terri Voepel-Lewis, M.S., R.N.; University of Michigan, Ann Arbor, MI.

PURPOSE: Serotonin 5-HT_3 receptor antagonists' agents have been shown to effectively reduce postoperative vomiting. This study evaluated the safety and efficacy of intravenous dolasetron 12.5 mg fixed dose vs. 0.35 mg/kg vs. placebo, in children undergoing strabismus surgery.
METHODS: Following IRB approval and parental consent, 118 patients aged 2-12 years old were randomized to receive placebo, dolasetron 12.5 mg, or 0.35 mg/kg 15 minutes prior to the end of surgery. Anesthesia was induced with halothane in N_2O/O_2 and maintained with isoflurane. Oral acetaminophen (15 mg/kg) was administered pre-operatively, and intravenous ketorolac (0.5 mg/kg) intraoperatively for analgesia. Post-operatively episodes of vomiting, time to awakening, PACU length of stay and agitation were recorded. Patients experiencing two or more episodes of vomiting were rescued with metoclopramide 0.05 mg/kg. Data were compared using unpaired t-tests, and Chi square with Fisher's exact test where appropriate.
RESULTS: Patients with an acute complete response (ACR) defined as no emetic episodes and no rescue medication within 24 hours of study drug administration were 62% (weight dose), 64% (fixed dose) and 33% (placebo, $p<0.05$). There was no statistical difference in ACR between the 0.35 mg/kg dose and the fixed 12.5 mg dose of dolasetron with both doses reducing the incidence of postoperative vomiting (POV).
CONCLUSION: Prophylactic administration of intravenous dolasetron reduced the incidence of postoperative vomiting following strabismus surgery. There was no statistical difference between a fixed dose and weight based dose. Prophylactic administration of dolasetron is well tolerated and effective for the prevention of POV in children.

Pharmacoeconomics

223. Blood pressure among hypertensive patients with diabetes: JNC-VI versus ADA guidelines. James Jackson, Pharm.D., Anne Frechette, R.N., BSN, Feride Frech, R.Ph., MPH, *Samantha Hibler*; Applied Health Outcomes; Novartis Pharmaceuticals Corporation, Tampa, FL.

PURPOSE: Risk of cardiovascular disease in hypertensive patients with diabetes is approximately two-fold greater than in those without diabetes. Controlling blood pressure (BP) with appropriate therapy is key to improving outcomes. Our objective was to compare the level of BP control among HTN-DM patients using the 1997 JNC-VI standard of 130/85 mm Hg versus the 2002 ADA recommendation of 130/80 mm Hg.
METHODS: As part of a national hypertension quality improvement program, chart reviews for 491 randomly selected HTN-DM patients in four major health care plans were conducted (1/99 to 10/01). BP control as defined by each guideline, cardiovascular risk factors, target organ damage, and antihypertensive therapy were analyzed using descriptive statistics.
RESULTS: The HTN-DM population was predominantly female (55%) and Caucasian (55%) with a mean age of 63. Compelling risk factors included dyslipidemia (70%), CAD/angina (14%), nephropathy (10%), retinopathy (10%), CHF (10%) and stroke/TIA (9%). Per JNC-VI, 26.2% of patients had controlled BP; using the new ADA guidelines, only 19.8% were controlled. Antihypertensive monotherapy was prescribed most often (37%), followed by treatment with two (34%) and three or more (25%) agents; 57% were on an ACEI while 12% were receiving an ARB.
CONCLUSION: BP is poorly controlled in HTN-DM patients. Given the importance of this high-risk population and the new BP goals, it is critical that physicians treat aggressively in order to control BP and reduce the high risk of adverse outcomes.

224. Nesiritide utilization and protocol development. *Jennifer D. Van Cura, Pharm.D.*; Cardinal Health Provider; King's Daughters Medical Center, Ashland, KY.

PURPOSE: In response to FDA approval of nesiritide, a proactive pharmacoeconomic analysis was needed to assess the utilization of this medication in clinical practice. The purpose is to determine the appropriate place in therapy of nesiritide.
METHODS: An assessment of nesiritide literature was performed and a medication use evaluation (MUE) is conducted for each patient receiving nesiritide at this institution, beginning September 2001. Patient demographics, drug management during admission, and clinical outcomes are assessed.
RESULTS: Upon evaluation of MUE results, it was determined that physicians were not utilizing significant doses of intravenous loop diuretics (15.8%), nor were they conducting trials of nitroglycerin in CHF patients prior to prescribing nesiritide (22.2%). Daily fluid input and output were not documented. The average length of nesiritide therapy was 4.57 days despite the lack of data on the benefits of utilization longer than 48 hours. The excess cost to patients who received the medication for longer than 48 hours was $31,418 over 3 months. Most orders (80%) were written “per pharmacy protocol” even though a pharmacy protocol did not exist. By developing a nesiritide protocol including daily input and output, intravenous loop diuretic therapy, a 48-hour stop, and a restriction to the cardiology department - an improvement in patient care and a significant patient savings was realized. Average length of therapy was reduced to 2.56 days since protocol implementation. With this reduction, there is an estimated per patient savings of approximately $2,000.
CONCLUSION: The implications of a nesiritide protocol include improved patient care and cost avoidance.

225. Improvement of angiotensin converting enzyme inhibitor utilization in diabetic Medicaid patients. *Melanie A. Dodd, Pharm.D., BCPS*; University of New Mexico, Albuquerque, NM.

PURPOSE: To educate prescribers and pharmacists on the use of angiotensin converting enzyme inhibitors (ACEI) in diabetic patients in order to slow the development and progression of diabetic nephropathy according to the American Diabetes Association position statement and to increase prescribing of ACEI in appropriate diabetic patients.
METHODS: Adult Medicaid fee-for-service patients with prescription claims for diabetic medications between August and October 1999 were identified. In February 2000, educational materials regarding the role of ACEI in diabetic nephropathy were mailed to the prescribers and pharmacists of diabetic patients not receiving ACEI (excluding pregnant patients). In addition, response forms and medical profiles were mailed to the providers for each patient. Prescribing changes in ACEI were evaluated three months and one year after the mailed intervention.
RESULTS: A total of 1996 patients, 778 prescribers, and 248 pharmacists were identified. At least one response form was returned on behalf of 47% of the patients, with 41% and 25% of the prescribers and pharmacists responding, respectively. At baseline 0% of the patients were receiving ACEI. Three months after the intervention 10% of the study patients were receiving ACEI, rising to 15% after one year.
CONCLUSIONS: A mailed intervention to healthcare providers was effective in improving ACEI utilization in Medicaid diabetic patients in accordance with evidence-based guidelines. Due to lack of diagnosis information it is unclear what percentage of these patients should be receiving ACEI. A cost effectiveness analysis of this intervention is currently in progress, which may provide health-policy implications for the Medicaid program.

226. Cost and effectiveness of venlafaxine extended-release and selective serotonin reuptake inhibitor treatment for major depression: workplace implications. Madhukar Trivedi, M.D., Roman Casciano, M.S., *George J. Wan, Ph.D., MPH*, Rajiv Mallick, Ph.D., Jieling Chen, M.A., Erika C. Geissler, R.N., M.B.A.; University of Texas Southwestern Medical Center, TX; Wyeth Research, St. Davids, PA.

PURPOSE: To estimate cost and effectiveness of venlafaxine extended-release (VENXR) and selective serotonin reuptake inhibitors (SSRIs) for major depression.
METHODS: A decision model was developed to estimate the cost and effectiveness of VENXR and SSRIs as measured by costs (pharmacy/medical) and effectiveness (patient achieving full activity/productive day). The probability of achieving full activity and number of productive days were based on pooled data from eight clinical trials comparing venlafaxine, SSRIs, and placebo over eight weeks of treatment. Medical costs over eight weeks of treatment were modeled using probabilities of symptom response from the pooled clinical trial data, associated therapy changes from an expert panel, and treatment costs from the 2002 HCCA Physician Fee and Coding Guide. Pharmacy costs and market share data were based on AWP listings from 2002 Red Book and 2001 IMS NPA Plus.
RESULTS: The cost per patient achieving full activity for VENXR was $2,260.50 versus $2,786.79 for SSRIs. The cost per productive day for VENXR was $26.54 versus $28.24 for SSRIs. The costs per patient achieving

full activity and productive day were computed using the expected mean total costs ($585.47 for VENXR; $546.21 for SSRIs), the probability of achieving full activity (25.9% for VENXR; 19.6% for SSRIs), and the expected productive days per patient (22.06 for VENXR; 19.34 for SSRIs).
CONCLUSIONS: VENXR positively impacts workplace efficiency including achievement of full activity and productive days. VENXR is a cost-effective treatment for major depression in terms of cost per patient achieving full activity and cost per productive day.

227. Impact on proton pump inhibitor utilization and costs following a pharmacy preference change and conversion. *B.A. Brown*, L.A. Kipley, P.A. Tabor, A.K. Thompson; Scott and White Health Plan, Temple, TX; Janssen Pharmaceuticals, Titusville, NJ.

PURPOSE: This study evaluates PPI pharmacy costs and daily tablets consumed (DACON) before and after a pharmacy policy conversion in which the preferred PPI changed from lansoprazole to rabeprazole.
METHODS: A retrospective claims-based analysis was undertaken in a managed care plan with approximately 167,000 members from March through December 2000. Outcomes were evaluated over two 4-month periods (pre- and post-conversion), and a 2-month conversion period. Wholesale acquisition costs were used. Paired t-tests assessed statistical significance in changes in PPI pharmacy costs and DACON among a subset of patients with equal numbers of pre/post PPI prescriptions.
RESULTS: PPI prescriptions totaled 24,873 in 6437 patients; 59% female, 83% between ages 18 and 75. Nine hundred nineteen patients had equal numbers of pre/post PPI prescriptions. In this subset, the average cost per prescription decreased $7.76 ± 35.86 ($p<0.0001$), and DACON decreased 0.02 ± 0.22 ($p<0.01$). Among 6437 patients, lansoprazole market share decreased (91% to 3%), while rabeprazole increased (3% to 90%); omeprazole share remained low (~7%), and pantoprazole was limited (< 1%). PPI DACON averaged (n = prescriptions): rabeprazole 1.06 (n=9854), lansoprazole 1.08 (n=13,157), omeprazole 1.07 (n=1768), pantoprazole 1.03 (n=94).
CONCLUSIONS: Conversion from lansoprazole to rabeprazole achieved in 90% of patients resulted in significant reductions in PPI pharmacy costs and DACON.

228E. Risk of first febrile neutropenia among patients receiving CHOP chemotherapy. *Gary H. Lyman, M.D.*, Vicki A. Morrison, M.D., David C. Dale, M.D., Jeffrey Crawford, M.D., David J. Delgado, Ph.D., Moshe Fridman, Ph.D.; Albany Medical Center, Albany, NY; VA Medical Center, Minneapolis, MN; University of Washington, Seattle, WA; Duke Medical Center, Durham, NC; Amgen, Thousand Oaks, CA; AMF Consulting, Los Angeles, CA.

Presented at the 38th Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 18-21, 2002.

229. Economic evaluation of clinical pharmacy services, 1996 – 2000. Melissa G. Butler, Pharm.D., *Glen T. Schumock, Pharm.D., M.B.A.*, Patrick D. Meek, Pharm.D., Lee C. Vermeulen, M.S., Bhakti V. Arendokar, M.S., Jerry L. Bauman, Pharm.D.; University of Illinois at Chicago, Chicago, IL; University of Wisconsin Hospital and Clinics, Madison, WI; University of Wisconsin-Madison, Madison, WI.

PURPOSE: The purpose of this analysis was to evaluate original evaluations of the economic impact of clinical pharmacy services (CPS) published from 1996-2000, and to provide recommendations for future research.
METHODS: Articles identified through a literature search were blinded and randomly assigned to reviewers to confirm inclusion and abstract information. Results were compared to a similar review of literature published between 1988 and 1995.
RESULTS: A variety of practice sites (hospitals, community pharmacies and clinics, health maintenance organizations, and long-term or intermediate care facilities) and CPS (general pharmacotherapeutic monitoring, target drug programs, disease state management, and patient education or cognitive services) were represented in the 59 included articles. Compared to the previous review, a greater proportion of evaluations were conducted in community pharmacies, clinics and non-US sites, contained more rigorous study designs, and represented comprehensive rather than specialized services. Articles were categorized by type of evaluation; 35.5% were outcome analyses, 23.7% full economic evaluations, 16.9% outcome descriptions, 15.2% cost-outcome descriptions, and 8.5% cost analyses. Most studies reported positive financial benefits. In 16 studies a benefit-to-cost ratio could be calculated (range: 1.7:1 to 17.0:1, median 4.68:1).
CONCLUSION: While the body of literature included in this review provides evidence of the continued economic benefit of CPS, the emergence of evaluations from community pharmacies and non-US countries is reflects the need to justify CPS in new and emerging frontiers. Despite improvement in the quality of study design, whenever possible, future evaluations should incorporate methodologies that will further enhance the strength of this literature and the conclusions drawn from it.

230. Effects of a coordination of care intervention on pharmacy and medical utilization in the Florida Medicaid population. *Robert Berringer, Pharm.D.*, Urvashi Patel, MPH; Heritage Information Systems, Inc., Richmond, VA.

PURPOSE: To improve coordination of care (COC) with provider and pharmacies for Medicaid fee-for-service patients at high risk for adverse events.
METHODS: Prospective pre/post study. Physicians of those patients that received more than 10 different medications, prescribed by ≥ 3 different providers, and dispensed at ≥ 3 different pharmacies in the most recent 60 days prior to baseline were targeted. Physicians were mailed a cover letter explaining the criteria, a patient newsletter, and patient profiles. Changes in pharmacy and medical utilization from baseline to 6 months were compared for those patients continuously enrolled during the post intervention period.
RESULTS: Three thousand three hundred and seventy seven patients had COC issues at baseline while only 769 (-77%) did at 6 months ($p<0.05$). At baseline the average unique medications, pharmacies, and physicians per patient were 14.3, 3.6, and 5.2, respectively. At 6 months, those patients that no longer had COC issues (n=2608) compared to those that did (n=769) had less average unique medications (11.2 vs. 15.6, respectively), pharmacies (2.3 vs. 3.7), and physicians (3.7 vs. 5.5). Changes from baseline were significant ($p<0.05$) for all parameters except the number of unique medications in those patients that still had COC issues. Additionally, the average cost per patient per month for prescriptions decreased 8.5% (-$56.53) while medical costs per patient per month decreased 53.0% (- $56.64). Overall cost avoidance from baseline to 6-months is $385,561.
CONCLUSIONS: By notifying physicians of patients with potential coordination of care issues, positive clinical and economic outcomes were seen.

Pharmacoepidemiology

231. Predicting initiation of statin therapy at Fallon Community Health Plan: building a propensity score-matched cohort study. *John D. Seeger, Pharm.D., Dr.PH.*, Alexander M. Walker, M.D., Dr.PH., Paige L. Williams, Ph.D., Frank M. Sacks, M.D., Gordon M. Saperia, M.D.; Harvard University, Boston, MA; Ingenix Epidemiology, Newton, MA; Fallon Clinic, Worcester, MA.

PURPOSE: National guidelines specify clinical characteristics that identify patients as candidates for statin therapy. We sought to identify empiric predictors of statin initiation and develop a propensity score that could be used to create matched cohorts.
METHODS: From 1993 through 1999, Fallon Community Health Plan members initiating statin therapy were compared to eligible non-initiators. Patient characteristics were compared across serial half-year blocks of calendar time both univariately (t-test or Fisher's exact test), and multivariately (logistic regression).
RESULTS: There were an average of 504 statin initiators and 8958 non-initiators in each half-year block. Statin initiators differed significantly from non-initiators on 43 of 52 variables evaluated with statin initiators exhibiting higher cardiovascular risk. Plasma lipid values (LDL, HDL, and TG) and cardiovascular comorbidities were highly predictive of statin initiation, while other NCEP variables (age, sex, diabetes, hypertension, and smoking) were less predictive. Variables relating to health care utilization (physician visits, laboratory tests, and prescription dispensings) were more predictive than many clinical variables. A logistic regression including all 52 variables discriminated well between statin initiators and non-initiators (c-statistic=0.92), and matching based on this model (propensity score) created cohorts (N=2901 each) that were significantly different from each other on only one of the 52 variables.
CONCLUSIONS: Among persons eligible for statin therapy, lipoprotein concentrations and cardiovascular comorbidities are predictive of statin initiation, but measures of healthcare utilization are equally predictive. Despite the existence of many highly predictive characteristics, the excess of non-initiators among the eligible patients permits propensity score matching to form balanced comparison cohorts suitable for the study of drug effects.

232. Risk factors for drug-related Stevens-Johnson syndrome and toxic epidermal necrolysis: a case-control study in Taiwan. *Mei-Shu Lin, M.S.*, Yang Shia Dai, M.D., Raoh-Fang Pwu, M.S., Yen-Hui Chen Ph.D.; National Taiwan University; National Taiwan University Hospital, Taipei, Taiwan.

PURPOSE: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, however, life-threatening cutaneous reactions. The etiology of SJS and TEN are usually drug-related (80~95 % of patients with TEN, >50 % with SJS). The purpose of this study is to estimate odds ratios of suspected drugs in Taiwan.
METHODS: A case-control study was used to estimate the odds ratios of suspected drugs related to SJS/TEN. The analysis of total subjects was based on 35 cases and 94 controls. The suspected cases of SJS or TEN were identified from the database of discharge files. And then, some of the suspected cases were classified as having SJS or TEN by case validation. Control subjects were randomly sampled from the same database with an acute condition, and drug-related E-codes were excluded. A control group with four subjects for each case was randomly sampled by matching age (± 2 years old), sex and admission month. We estimated odds ratios with multivariate analysis.

RESULTS: Carbamazepine has the most strong association with SJS/TEN (OR=28.1; CI 3.6, 220). The odds ratios for allopurinol and phenytoin were 17.6 (CI 2.1, 149.4) and 7.4 (CI 1.5, 37.5), respectively. The death rates of SJS and TEN were 10% and 40%, respectively. The average onset of these severe conditions after initial drug administration was 15 days.
CONCLUSIONS: This study, with limited sample sizes, observed that carbamazepine, allopurinol, and phenytoin increase the risk of SJS and TEN. Further study with larger sample size is needed to confirm the results.

233. *Streptococcus pneumoniae* susceptibility to cefotaxime and ceftriaxone, 1995-2001: national and regional trends from the Antimicrobial Resistance Management program. *John G. Gums, Pharm.D.*; University of Florida, Gainesville, FL.

PURPOSE: *S. pneumoniae* is the leading cause of community-acquired pneumonia and pneumococcal bacteremia. Using data from the ongoing Antimicrobial Resistance Management (ARM) program, this study examined national and regional susceptibility rates of *S. pneumoniae* to two second-generation cephalosporins, cefotaxime and ceftriaxone, historically regarded as being therapeutically equivalent.
METHODS: The ARM program has collected nearly 15 million inpatient and outpatient isolates from 121 hospitals in five U.S. regions: north central, northeast, south central, southeast, southwest. Antibiograms and sensitivity reports of pneumococcal isolates collected from 1995-2001 were reviewed for susceptibility to cefotaxime and ceftriaxone and compared using a Web-based analysis tool.
RESULTS: From 1995-2001 nationally, *S. pneumoniae* isolates were more susceptible to ceftriaxone (80.9%, n=16,944) than to cefotaxime (71.7%, n=4366). This difference was accounted for primarily in the Southeast (cefotaxime, 65%; ceftriaxone, 77.7%). Rates were consistently lower for cefotaxime for each of the years reviewed. In 1995, susceptibility was 54.7% (n=347), compared with 75.2% (n=997) for ceftriaxone; and, for 2001, 73.6% (n=338) compared with 82.3% (n=499) for ceftriaxone. Regionally, this trend was seen in all areas except in Northeast, where rates were comparable, with the exception of 2001: susceptibility to cefotaxime was 70.2% (n=212), compared with 80.7% for ceftriaxone (n=285).
CONCLUSIONS: These data suggest that cefotaxime and ceftriaxone may not be therapeutically equivalent for the treatment of *S. pneumoniae*. Given the recent change in recommended breakpoints for these two third-generation cephalosporins, this information may have clinical relevance.

234. Ambulatory care medication dose adjustments in renal insufficiency: can we do better? *Charron L. Long, Pharm.D.*, David J. Magid, M.D., MPH, Marsha A. Raebel, Pharm.D., BCPS, Elizabeth A. Chester, Pharm.D., BCPS, Ella E. Lyons, M.S.; Kaiser Permanente, Aurora, CO.

PURPOSE: There is little data regarding adherence with dosing adjustment recommendations for renal insufficiency (RI) in the ambulatory setting. This study describes adherence to medication dosing recommendations in ambulatory patients with renal insufficiency in a group model HMO.
METHODS: Medications requiring dose adjustment in RI were identified. Occurrences of prescribing for these medications in RI were then defined using a CrCl < 50 (Cockroft and Gault). In cases where a medication was prescribed in RI, the actual dose prescribed was compared to the recommended adjusted dose (based on the patient's creatinine clearance). A subset of 20 select medications requiring dosage adjustment for patients with RI were identified by an expert panel for further intervention, based on frequency of use and perceived potential for adverse clinical outcomes.
RESULTS: One hundred thirty-three medications requiring renal dosing adjustment were identified. Over a three-month period, 64 of those medications (a total of 2134 occurrences) were prescribed in a renal insufficient patient within our system. Overall, 1098 (51.4%) of the prescriptions were potentially dosed excessively. Of the 20 select medications, there were 514 occurrences of prescribing in a patient with RI. In 358 (69.6%) of those cases, the medication was dosed higher than recommended based on the patient's creatinine clearance. Medications dispensed more frequently and potentially dispensed inappropriately include allopurinol, ranitidine, metformin, gabapentin, nitrofurantoin, and glyburide.
CONCLUSIONS: Our study shows ambulatory care physicians often fail to adjust medication dosages for patients with renal insufficiency. The clinical implications of this excessive dosing should be further explored.

235. Antidepressant adherence in the Iowa Medicaid pharmaceutical case management population. *Ryan M. Carnahan, Pharm.D.*, Brian C. Lund, Pharm.D., M.S., BCCP, Elizabeth A. Chrischilles, Ph.D., Paul J. Perry, Ph.D., BCCP; University of Iowa, Iowa City, IA.

PURPOSE: To describe the extent of and factors related to medication adherence among patients treated with antidepressants in the Iowa Medicaid Pharmaceutical Case Management Program.
METHODS: Fills for antidepressant medications and a selected group of chronic non-antidepressant medications (e.g. antihypertensives, lipid-lowering agents, etc.) were identified from electronic pharmacy claims over a one year period. Adherence was measured using a standardized method and defined as the number of days during the treatment period that the patient was observed to be without a supply of medication (MED-OUT).
RESULTS: This analysis included 2200 patients who received either an antidepressant or one of the selected chronic medications. Of the 1210 antidepressant users, 75% were adherent as defined by a threshold MED-OUT value of ≤ 0.20 (80% compliant). Antidepressant adherence did not differ across pharmacologic class (p=0.23) or gender (p=0.22), but improved significantly with increasing age (p=0.006). Furthermore, adherence did not differ between antidepressants and chronic medications among patients receiving both (0.14 vs. 0.12, respectively; p=0.56).
Finally, adherence to chronic medications was compared between antidepressant users and non-users. While adherence was impaired among antidepressant users (p=0.023), this effect was significantly dependent on age (p=0.032). In other words, antidepressant use was associated with better medication compliance in younger patients (≤ 55 years), but worse medication compliance among older patients.
CONCLUSIONS: Prior research suggests that patients with depression are at risk for non-compliance. While this finding was supported in the current study among the elderly, younger patients treated with antidepressants actually displayed better overall medication adherence. This observation has important implications for future compliance research in depression.

236E. Antipsychotic drugs and the risk of cardiac arrest and ventricular arrhythmia. *Sean Hennessy, Pharm.D., Ph.D.*, Warren B. Bilker, Ph.D., Jill S. Knauss, M.S., David J. Margolis, M.D., Ph.D., Stephen E. Kimmel, M.D., MSCE, Robert F. Reynolds, Ph.D., Dale B. Glasser, Ph.D., Mary F. Morrison, M.D., MSCE, Brian L. Strom, M.D., MPH; University of Pennsylvania, Philadelphia, PA.

Presented at the 2001 Annual Meeting of the American Psychiatric Association, New Orleans, LA, May 5-10, 2001.

237. Time to discontinuation of nonsteroidal anti-inflammatory drugs among patients with rheumatoid arthritis and osteoarthritis. *Kristijan H. Kahler, R.Ph., S.M.*, Douglas Gause, M.S., Dr.PH., Winnie Zhang, M.D., M.S.; Novartis Pharmaceuticals, East Hanover, NJ.

PURPOSE: Describe differences in the time to discontinuation for various nonsteroidal anti-inflammatory drugs (NSAIDs) among patients newly treated for rheumatoid arthritis (RA) and osteoarthritis (OA).
METHODS: Data were extracted from Medstat's MarketScan, a proprietary claims database. From those continuously enrolled and with an RA or OA claim (ICD9 = 714.xx or 715.xx) between July 1999 to December 2000, we identified patients with an initial prescription for an NSAID during 2000 with none prescribed in the last six months of 1999. Kaplan-Meier curves were created to assess the time to discontinuation for the following drug groups: rofecoxib®, celecoxib (C), meloxicam (M), diclofenac plus misoprostol (A), and all others (O).
RESULTS: This analysis consisted of 32,807 patients with RA or OA starting NSAID therapy. The COX-2 selective inhibitors, rofecoxib and celecoxib accounted for 59.7% of initial prescriptions. The median time to discontinuation was greatest for R at 65 days, and for M, C, A, and O was 60, 57, 47, and 42, respectively. Rofecoxib, celecoxib, and to a lesser extent, meloxicam appeared to have better persistency than the traditional NSAIDs. There was a sharp increase in discontinuation after the initial 30 day supply of medication for all products.
CONCLUSION: The COX-2 selective agents appear to offer improvements over the traditional NSAIDs with regard to persistency, however, compared to other maintenance medication classes, the time to discontinuation for NSAIDs is still low. There is a need for medications that offer improved tolerability or efficacy, or both.

238. Geographical Information Systems and drug utilization: acute sinusitis therapy. *Julie J. Wilkinson, Pharm.D.*, R.W. Force, B. Novak, C. Kelley; Idaho State University, Pocatello, ID.

PURPOSE: To evaluate geospatial relationships of appropriate and inappropriate antibiotic use for acute sinusitis in one state's Medicaid population.
METHODS: A Medicaid database was queried over a one-year timeframe to identify cases of acute sinusitis with an antibiotic dispensed within two days of diagnosis. Prescription claims data were gathered including name and address for patient and provider, diagnosis code, antibiotic name, and cost of therapy. Each case was classified as appropriate or inappropriate according to sinusitis recommendations from a 2001 clinical practice guideline from the American College of Physicians – American Society of Internal Medicine. Amoxicillin, doxycycline, and sulfamethoxazole/trimethoprim were considered appropriate. Geographical Information Systems software (ArcGIS® v8.2) was used to join our claims data with a coverage of state ZIP codes. Tools in ArcGIS were used to create individual bar graphs for each ZIP code that contained at least ten cases. The size of each bar graph indicated the total cases of treated sinusitis. Color-coding represented the fraction of appropriate and inappropriate prescriptions.
RESULTS: A map was created to provide a visual representation of sinusitis prescribing (3026 cases) across the state. Fifty-four of 293 ZIP codes contained at least ten cases each. Within those 54 ZIP codes, 2918 cases

(96.4%) were mapped. Across the state, 65.0% of cases were treated with an inappropriate antibiotic. Visual evaluation of the map indicated substantial variability of appropriate prescribing.
CONCLUSIONS: Geographical Information Systems provided an excellent tool for evaluating antibiotic therapy for acute sinusitis on a statewide basis. This technology offers enhanced perspective of drug use patterns across a defined geographical area.

Pharmacogenomics/Pharmacogenetics

239. The effect of CYP3A4*1B 5'-promoter region polymorphism on cyclosporine pharmacokinetics among healthy volunteers. *David I. Min, Pharm.D., FCCP,* Vicki L. Ellingrod, Pharm.D., BCPP; University of Iowa, Iowa City, IA.

Cyclosporine(CsA) is a substrate for CYP3A4 and MDR1 gene product, p-glycoprotein (P-gp) and its pharmacokinetics is influenced by various factors including these genotypes. Recently, functional polymorphisms of the CYP3A4*1B 5'-promoter region and C3435T of MDR1 gene have been reported.
PURPOSE: To determine the effect of CYP3A4*1B 5'-promoter region polymorphism on CsA pharmacokinetics among healthy volunteers.
METHODS: The pharmacokinetic study of oral CsA was performed in 14 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 CYP3A4 and MDR1 polymorphism using the polymerase chain reaction and a restriction digest. Each CsA pharmacokinetic parameters were compared using one-way ANOVA test.
RESULTS: There were four (4) homozygous A/A (wild type), four (4) homozygous G/G (variant) and six (6) heterozygous A/G genotypes for CYP3A4 in these 14 healthy volunteers. For MDR1 genotype, there were seven (7) homozygous C/C, six (6) C/T and one (1) homozygous T/T genotypes in these 14 healthy volunteers. All of subjects with homozygous A/A genotype of CYP3A4 were MDR1 C/T heterozygous and most of subjects with CYP3A4 homozygous G/G genotypes were MDR1 C/C homozygous genotype. According to the genotypes of CYP3A4, the mean pharmacokinetic parameters (± SD) of oral cyclosporine are as follows.

	A/A (wild)	G/G (variant)	A/G	P value
T_{max} (hour)	1.8 ± 0.3	1.9 ± 0.7	1.7 ± 0.5	0.8
C_{max} (ng/ml)	1721 ± 755	1094 ± 243	1481 ± 458	0.264
$T_{1/2}$ (hour)	7.6 ± 4.3	6.9 ± 3.6	5.9 ± 0.9	0.680
AUC (ng•hour/ml)	6989 ± 1945	4634 ± 1022	6886 ± 1619	0.0432*
CL/F (l/hour)	49.4 ± 13.9	83.5 ± 16.0	52.5 ± 5.6	0.0024*

CONCLUSIONS: The CYP3A4*1B 5'-promoter region polymorphism appears to influence AUC and CL/F of oral CsA significantly in healthy subjects. Further study with larger sample size may be needed to confirm these results.

240. Adrenergic receptor polymorphisms and response to dobutamine. *Christina L. Aquilante, Pharm.D.,* Larisa M. Humma, Pharm.D., Steven G. Terra, Pharm.D., Tara M. Andrisin, B.S., Jannet F. Lewis, M.D., Karen K. Hamilton, M.D., Joseph Walker, Pharm.D., Leslie Picoult-Newberg, Ph.D., Julie A. Johnson, Pharm.D.; University of Florida, Gainesville, FL; University of Illinois at Chicago, Chicago, IL; Orchid BioSciences, Princeton, NJ.

PURPOSE: Non-synonymous single nucleotide polymorphisms commonly occur in the β_1, β_2, and α_{1A} adrenergic receptor genes at codons 49 and 389 (β_1AR), codons 16 and 27 (β_2AR), and codon 492 (α_{1A}AR). We evaluated whether these polymorphisms affected hemodynamic response to dobutamine during dobutamine stress echocardiography (DSE).
METHODS: One hundred thirty-two patients underwent DSE with dobutamine dose titrated from 5 to 40 µg/kg/min until target heart rate (HR) was reached or symptoms developed. Blood pressure and HR data were recorded at rest and at the end of each dobutamine infusion rate. The E_{max} model was fitted to dobutamine dose-HR data using WinNonlin® software. Genotypes were determined using Orchid BioSciences' proprietary primer extension technology (SNP-IT)™.
RESULTS: Data for β_1AR codon 389 (n=108) and β_2AR codon 16 (n=132) are shown. There were no significant associations between any of the parameters tested and β_1AR codon 49, β_2AR codon 27, or α_{1A}AR codon 492 genotypes.

	β_1AR Codon 389		β_2AR Codon 16		
	Arg/Arg (n=57)	Gly Carriers (n=51)	Arg/Arg (n=24)	Arg/Gly (n=63)	Gly/Gly (n=45)
Resting HR (bpm)	81 ± 12	76 ± 11*	81 ± 12	78 ± 13	78 ± 12
Resting SBP (mm Hg)	153 ± 24	142 ± 28*	133 ± 25	149 ± 27‡	147 ± 26‡
Resting DBP (mm Hg)	83 ± 12	77 ± 14*	74 ± 13	81 ± 13‡	80 ± 13‡
ED_{50} (µg/kg/min)	17 ± 6	21 ± 7*	21 ± 6	17 ± 6	21 ± 5
E_{max} (bpm)	135 ± 24	138 ± 22	136 ± 21	132 ± 25	139 ± 21

Mean ± SD; ED_{50}=dose producing half-maximal response; E_{max}=maximal response; *, ‡p<0.05

CONCLUSION: β_2AR and α_{1A}AR genotype do not appear to influence hemodynamic response to dobutamine. Lower ED_{50} for β_1AR Arg389 homozygotes suggests greater sensitivity of this receptor to β_1AR agonists. These findings suggest that β_1AR codon 389 genotype influences response to β_1AR agonists used for stress testing and inotropic support.

242. Single nucleotide polymorphism genotyping of select genes in topotecan-treated children. *Lisa C. Iacono, Pharm.D.,* Charis P. Zamber, Ph.D., Elaine D. Odle, Erin G. Schuetz, Ph.D., Clinton F. Stewart, Pharm.D.; St. Jude Children's Research Hospital, Memphis, TN.

PURPOSE: We have previously shown that topotecan systemic clearance has wide inter-patient variability, which may be accounted for by several patient characteristics. However, the contribution of pharmacogenetics to inter-patient variability has not been studied. The goals of this study were to perform single nucleotide polymorphism (SNP) genotyping of select genes associated with topotecan clearance and relate patient genotype to topotecan disposition.
METHOD: DNA from peripheral blood mononuclear cells was obtained using standard techniques from children treated with topotecan. Genes associated with topotecan clearance were analyzed for commonly associated SNPs using polymerase chain reaction (PCR), sequencing, and polyphred analysis.
RESULTS: Genomic DNA was obtained from 38 children. As topotecan is a substrate for ABCG2, we examined SNPs in exon 2 in 35 children and exon 5 in 18 children. Four of five patients which had an exon 2 SNP at amino acid 12 (VàM) were heterozygous. Each of three patients which had an exon 5 SNP at amino acid 141 (N àK) were heterozygous.
CONCLUSION: Our patients had a 8.6% allele frequency of the exon 2 SNP and an 8.3% allele frequency of the exon 5 SNP, which is comparable to literature values. Comparison of these genotypes with topotecan pharmacokinetic phenotype is underway. Also, we continue to collect genomic DNA from additional children treated with topotecan. SNP genotyping is also being performed for the CYP3A4/5 gene as well as other drug transporters, such as ABCC4 and ABCB1.

243. Pharmacogenetics of thalidomide: drug response, in vivo metabolism and genetic polymorphism of CYP2C19. Yuichi Ando, M.D., Ph.D., Doug K. Price, Ph.D., William L. Dahut, M.D., Michael C. Cox, Pharm.D., Eddie Reed, M.D., *William D. Figg, Pharm.D.*; National Cancer Institute, Bethesda, MD.

PURPOSE: It has been known that thalidomide requires microsomal cytochrome P450 (CYP)-catalyzed biotransformation for its pharmacological activities, including antiangiogenic effect. It has been found that CYP2C19 is primarily responsible for 5- and 5'- hydroxylation of thalidomide. Because CYP2C19 is polymorphic enzyme, genotyping CYP2C19 gene of each patient might segregate the patient population into subgroups that differ in their ability to respond to thalidomide. This study was conducted to investigate the associations between the CYP2C19 genotype and clinical outcomes of thalidomide therapy.
METHODS: A case-control study of 63 patients with prostate cancer who were entered in the recent thalidomide phase II study at the NCI was explored. The genotype was observed by PCR-RFLP and the metabolite concentrations in plasma were measured by HPLC.
RESULTS: Two of the 63 patients were homozygous for the variant CYP2C19*2 allele and were considered as poor metabolizers. Both the patients were included in the 25 patients whose PSA declined <10% (non-responder) and the metabolite concentrations in plasma from both the patients were under the quantifiable levels showing inability of metabolite formation. No apparent association was found between the 14 heterozygotes (phenotypic extensive metabolizer) and PSA decline or in vivo metabolism. None of these patients had CYP2C19*3 or CYP2C19*4 alleles.
CONCLUSION: The findings were consistent with the hypothesis that a patient having the poor metabolizer genotype of CYP2C19 could receive little benefit from thalidomide treatment and that the poor metabolizer genotype is associated with lower ability of the metabolite formation.

Pharmacokinetics/Pharmacodynamics/ Pharmacometrics/Drug Metabolism

244. Carbapenem pharmacodynamics against common pathogens utilizing variability in pharmacokinetic parameters. *Kevin A. Enzweiler, Pharm.D.,* John A. Bosso, Pharm.D., Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To assess the impact of variation in pharmacokinetic (PK) parameters on the comparison of the pharmacodynamics (PD) of carbapenems (CP) against various organisms
METHODS: PK parameters obtained from 27 studies involving 220 subjects in peer-reviewed publications were used to simulate unbound serum concentration-time profiles in a 70 kg adult for IV imipenem (I), meropenem (M), and ertapenem (E). Variability in Cl was accounted for using published Cl vs. CrCl relationships; variability in Vss was accounted for with use of values from normal volunteer data reflecting mean ± 1 SD. MIC_{50} and MIC_{90} values were obtained from N. American studies published from 2000-2002 for

2 Gram-positive and 5 Gram-negative aerobes, and *B. fragilis* (13,060 drug/isolate pairs). Weighted (based on # of isolates) geometric mean MICs were used for subsequent PD calculations. Using manufacturer-recommended and non-approved regimens (I at approved doses of M and M at approved doses of I) with recommended dosage adjustments for renal dysfunction, simulations were performed at CrCl of 100, 75, 50, and 25 ml/min (51 regimens). Regimens were categorized as acceptable or optimal for all bacteria if the %T > MIC was ≥ 25 and 50, respectively.
RESULTS: Over the studied CrCl range using mean Vss, the % acceptable rank order was M = I > E for both MIC_{50} and MIC_{90}. M was 100% optimal for all organisms except *P. aeruginosa* and was differentiated from both I and E (M=59%, I=45%, E = 0% acceptable). Although simulations utilizing variations in Vss resulted in differences in %T > MIC, PD categorical results were not different. Although there was a trend towards increasing %T > MIC as CrCl declined, the categorical results were similar to those found in simulations at CrCl = 100 ml/min.
CONCLUSION: With the exception of *P. aeruginosa*, these CP exhibited similar PD profiles even when considering variability in renal function and Vss.

245. Murine pharmacokinetics and metabolism of oleandrin, a cytotoxic component of *Nerium oleander*. *Dan Ni, M.D.*, Timothy L. Madden, Pharm.D., Mary Johansen, Pharm.D., Edward Felix, M.S., Dah H. Ho, Ph.D., Robert A. Newman, Ph.D.; University of Texas, Houston, TX.

PURPOSE: (1) To evaluate the pharmacokinetics and metabolism of oleandrin in mice after intravenous (IV) and oral (PO) administrations of ^{3}H-oleandrin. (2) To investigate the brain tissue distribution of oleandrin after intraperitoneal.(i.p.) injection of either oleandrin or oleander extract.
METHODS: Analysis of oleandrin and its metabolites in plasma, urine, feces, and tissues was achieved by HPLC with radioactivity detector. Brain and plasma were analyzed by LC/MS/MS for oleandrin content after i.p. of drugs. Pharmacokinetic parameters were estimated by WinNonlin 3.1.
RESULTS: Oleandrin was rapidly absorbed after oral dosing with T_{max} at 20 min. The elimination half-life was longer (2.3 ± 0.5 h) than that after IV dosing (0.4 ± 0.1 h). An oral bioavailability of oleandrin was approximately 30%. After IV, the concentration of oleandrin in liver was approximately twice that measured in heart and kidney tissue. A major metabolite, oleandrigenin was found in these tissues. At 5 min after IV dosing, more than 60% of the total radioactivity in liver was oleandrin, while 28% of the given dose was present as oleandrigenin. Only oleandrin, but no oleandrigenin, was found in brain. Twenty-four hours following injection, 66% of the total injected radioactivity was found in feces. About 8% of total radioactivity were excreted in the urine.
CONCLUSION: Oleandrin was rapidly absorbed and distributed in mice. The major metabolite of oleandrin was oleandrigenin. Oleandrin was mainly eliminated by the liver and there were higher excretion in feces than in urine. The amount of oleandrin in brain tissue was higher after i.p. injection of oleander extract than that after injection of oleandrin.

246. Effect of ethanol on oral cocaine pharmacokinetics. *Robert B. Parker, Pharm.D.*, Naomi Gades, D.V.M., Timothy Mandrell, D.V.M., S. Casey Laizure, Pharm.D.; University of Tennessee; St. Jude Children's Research Hospital, Memphis, TN.

PURPOSE: Cocaine (C) is frequently ingested by nasal insufflation. However, only a small fraction of the dose is absorbed nasally with most of the drug being swallowed and then absorbed in the GI tract. Most cocaine users co-ingest ethanol (EtOH) which has been shown to inhibit hepatic carboxylesterase-mediated cocaine metabolism to benzoylecgonine (BE), and result in formation of the active metabolite, cocaethylene. Therefore, the purpose of this study was to determine the effect of EtOH on oral C pharmacokinetics in conscious dogs.
METHODS: Five adult, conditioned mongrel dogs received 4 mg/kg oral C, 4 mg/kg oral C preceded by 1 gm/kg IV EtOH, and 3 mg/kg IV C on different study days separated by at least 48 hours. C and metabolite concentrations were determined by HPLC. Pharmacokinetic parameters were determined by non-compartmental methods.
RESULTS: Pharmacokinetic parameters are summarized below. AUC values for IV cocaine are normalized to a dose of 4 mg/kg.

	Oral Cocaine	Oral Cocaine + EtOH	IV Cocaine
CL (l/min)	5.6 ± 1.8	1.4 ± 0.4*	1.0 ± 0.2*
$t_{1/2}$ (min)	85.2 ± 6.6	84.2 ± 9.1	74.9 ± 16.7
Cmax (ng/ml)	116 ± 98	331 ± 131*	2677 ± 299*
Bioavailability	0.18 ± 0.05	0.72 ± 0.17*	--
C $AUC_{0-\infty}$ (mg•min/l)	15.0 ± 4.7	58.6 ± 10.0*	83.1 ± 15.4*
BE $AUC_{0-\infty}$ (mg•min/l)	171.9 ± 45.5	409.9 ± 82.1*	357.4 ± 121.7*
AUC BE/AUC C	11.9 ± 3.4	7.1 ± 1.5*	4.19 ± 0.70*

*p<0.05 compared to oral cocaine by repeated measures ANOVA; data are presented as mean ± SD

CONCLUSIONS: 1) Oral C undergoes significant first-pass metabolism; 2) EtOH markedly inhibits first-pass C metabolism via a reduction in carboxylesterase-mediated formation of BE; 3) For oral C, the reduced AUC BE/AUC C ratio with EtOH with no change in $t_{1/2}$ suggests EtOH also inhibits intestinal carboxylesterases; 4) Intestinal metabolism may play a significant role in elimination of cocaine reaching the GI tract.

247. Pharmacoscintigraphic assessment of the regional drug absorption of M100240 in healthy volunteers. *Nancy E. Martin, Pharm.D.*, Kathryn A. Read, M.T., Louis Martin, Ph.D., Sriram Krishnaswami, Ph.D., Heather Wray, M.D., Jeff Barrett, Ph.D., FCP; Aventis Pharmaceuticals, Bridgewater, NJ; Pharmaceutical Profiles, Ltd, Nottingham, United Kingdom.

PURPOSE: M100240, a thioester of MDL100,173, is a dual ACE/NEP inhibitor currently in Phase II development. This study evaluated the relative bioavailability of M100240 in various regions of the gastrointestinal tract using the Enterion™ capsule in order to explore the absorption characteristics of M100240. The absolute bioavailability of M100240 was also assessed.
METHODS: Pharmacokinetic data were obtained from 13 healthy subjects in an open-label, single-dose, randomized, 5-period crossover study. Treatments included 25 mg M100240 via short intravenous infusion, oral immediate release tablet, and oral Enterion capsule delivery of drug substance to the proximal small bowel, distal small bowel, and ascending colon. Each treatment was separated by a 14-day washout period. The Enterion capsule was monitored throughout the gastrointestinal tract using scintigraphic imaging. M100240 and MDL100,173 plasma concentrations were quantified using a validated LC/MS/MS method and pharmacokinetic parameters were calculated using non-compartmental methods.
RESULTS: MDL100,173 C_{max} and AUC_{0-24h} following release in the proximal and distal small bowel are similar to estimates for the immediate release tablet. However, after release in the ascending colon, C_{max} and AUC_{0-24h} are decreased to approximately 13% and 41% of the corresponding estimates for the immediate release tablet. The estimates of relative bioavailability in the proximal small bowel, distal small bowel, and ascending colon relative to the oral immediate release tablet are 94%, 97%, and 41%, respectively. The absolute bioavailability estimate of M100240 is 49%.
CONCLUSION: M100240 is well absorbed throughout the proximal and distal small bowel with modest absorption in the ascending colon.

248. Effect of capsaicin on the pharmacokinetics and pharmacodynamics of warfarin in rats. *Hsiang-Yin Chen, M.S., Pharm.D.*, Shih-Hsien Chang, B.S., Chia-Feng Lai, M.S., Chia-Chun Chang, B.S., Fei-Yuan Hsiao, M.S. candidate; Taipei Medical University; Taipei Municipal Wan-Fang Hospital, Taipei, Taiwan.

PURPOSE: To evaluate the possibility of interaction between capsaicin and warfarin, the influence of capsaicin on the pharmacokinetic and pharmacodynamic parameters of warfarin was studied in Sprague Dawley rats.
METHODS: The pharmacokinetic study included a single dose model using an oral dose of warfarin at 2 mg/kg with placebo or an oral dose of capsaicin at 50 mg/kg; and a multiple dose model using warfarin at 0.2 mg/kg once daily with placebo or capsaicin at 50 mg/kg daily for 6 days. The plasma concentrations of warfarin were compared by a validated HPLC assay. The pharmacodynamic study used a single dose of warfarin (0.8 mg/kg) at day 4, with placebo or capsaicin at 50 mg/kg for 6 days. The levels of International normalized ratio (INR), employed as a pharmacodynamic index, were measured at day 1, 4, 5, 6.
RESULTS: Single dose of capsaicin resulted in 50% increase in the peak plasma concentration (C_{max}) of warfarin from 5.00 ± 2.14 to 7.31 ± 2.02 μg/ml, and area under concentration-time curves (AUC) from 97.66 ± 38.65 to 152.93 ± 33.52 μg•hr/ml (all $p<0.05$). In the multiple dosing model, significantly increased C_{max} and decreased clearance were also observed in the presence of capsaicin. Additionally, capsaicin significantly increased maximal INR from 2.66 ± 1.30 to 3.46 ± 1.44.
CONCLUSIONS: The significant pharmacokinetic and pharmacodynamic findings in rats highlight the possibility of interactions in human. Careful monitoring of PT with appropriate dose titration with warfarin may be needed with oral intake of capsaicin.

249E. Bioavailability of intranasal butorphanol using unit-dose sprayers in healthy volunteers. *George A. Davis, Pharm.D.*, Anita C. Rudy, Ph.D., Sanford M. Archer, M.D., Daniel P. Wermeling, Pharm.D.; University of Kentucky; Intranasal Technology, Inc., Lexington, KY.

Presented at the 31st Annual Meeting of the American College of Clinical Pharmacology, San Francisco, CA, September 20-23, 2002.

250E. Pharmacokinetic comparison of oxcarbazepine oral suspension formulation versus film-coated tablets. *J. D'Souza, Ph.D.*, G. Flesch, M.D.; Novartis Pharmaceuticals, East Hanover, NJ; Novartis Pharmaceuticals, Basel, Switzerland.

Presented at the 55th Annual Meeting of the American Epilepsy Society, Philadelphia, PA, November 2001.

251E. Pharmacokinetic modeling to determine effective doses of oxcarbazepine as monotherapy in children. *J. D'Souza, Ph.D.*, J. Needleman, Ph.D., A. Wong, M.S.; Novartis Pharmaceuticals, East Hanover, NJ.

Presented at the 55th Annual Meeting of the American Epilepsy Society, Philadelphia, PA, November 2001.

252E. Consistent pharmacokinetics of ximelagatran, an oral direct thrombin inhibitor, in patients with non-valvular atrial fibrillation and age- and gender-matched controls. Maria Wollbratt, M.Sc., *Ulf G. Eriksson, Ph.D.*, Michael Wolzt, Ph.D., Mia Svensson, M.Sc., Karin Wahlander, M.D., Ph.D., Margaretha Grind, M.D., Ph.D.; AstraZeneca R&D, Molndal, Sweden; University of Vienna, Vienna, Austria; AstraZeneca R&D, Loughborough, United Kingdom.

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253. Eye movements during same day repeated testing. *M. Maggie Folan, R.N., B.S.N.*, Patricia D. Kroboth, Ph.D., Tanya J. Fabian, Pharm.D., Frank J. Kroboth, M.D., Gretchen Haas, Ph.D., Roslyn A. Stone, Ph.D., Kristin L. Bigos, B.S., John A. Sweeney, Ph.D.; University of Pittsburgh, Pittsburgh, PA; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Saccadic eye movements (SEMs) are frequently used as measures of central nervous system activity as a quantitative indicator of drug response. This study evaluated the influence of time on SEM dynamics (velocity, amplitude, latency, gain) in healthy young and elderly women and men.
METHODS: The 66 volunteers were medically and psychiatrically healthy women (18 young and 14 older) and men (22 young and 12 older). Ages ranged from 20 to 30 years (young) and 66 to 78 years (older). Visually guided SEM recordings to multiple targets (8° and 16° of vision to the right and left of center fixation) were obtained using an infrared reflection technique at 10 testing sessions over 12.5 hours. A repeated measure ANOVA was used to assess the differences in SEM dynamics over time.
RESULTS: Latency was stable over 12.5 hours for both groups. In the young, velocity was stable over time, while amplitude (to 16° targets) and gain (to 8° and 16° targets) improved ($p \leq 0.03$). In the older group, velocity to 8° targets varied over time ($p=0.04$). For all target locations, velocity, amplitude, and gain were greater and latency was lower in the young ($p \leq 0.02$).
CONCLUSIONS: SEM dynamics are relatively stable for ten repeated testing sessions during 12.5 hours. However, when used as a measure of drug response, inclusion of a placebo treatment is necessary to account for time-associated learning, especially in the young. When SEM dynamics differed statistically across time, the young group showed improvement while the older group was more variable.

254. Pharmacokinetics and dose proportionality of tazarotene following oral administration in healthy subjects. *Edward Lee, Ph.D.*, Lisa M. Borbridge, M.S., Patricia Walker, M.D., Ajit Suri, Ph.D., Diane D.S. Tang-Liu, Ph.D., Dale K. Yu, Ph.D.; Allergan, Irvine, CA.; Eli Lilly & Co., Indianapolis, IN.

PURPOSE: The pharmacokinetic profiles of tazarotene and its primary active metabolite, tazarotenic acid were evaluated following increasing single and multiple doses of oral tazarotene.
METHODS: This was a single-center, open-label, stratified, randomized, two-period, parallel-group, single- and multiple-dose, dose-proportionality pharmacokinetic study in which 41 healthy volunteers were assigned to received 3 mg, 6.3 mg, 6.3 mg with food, 9 mg, or 12 mg tazarotene. After a single dose and after 7 days of dosing, plasma samples (and skin at one time-point) were collected over a 72-hour period for determination of drug concentrations using a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using a non-compartmental approach. Effect of dose, food, and gender on the pharmacokinetics of tazarotene and tazarotenic acid were evaluated.
RESULTS: Tazarotene was present only in minute quantities, with the major drug related species being tazarotenic acid. Following multiple doses, tazarotenic acid AUC values were similar to single dose values and increased approximately proportionally to dose ($p = 0.08$). Tazarotenic acid C_{max} and AUC values were not different between fasted and fed treatments (90% confidence interval) or between genders ($p = 0.11 - 0.25$). Tazarotenic acid in skin biopsy samples collected from volunteers ranged from 21 to 40 ng/g.
CONCLUSIONS: The pharmacokinetics of tazarotenic acid after a single dose was predictive of steady-state kinetics, and systemic exposure was approximately proportional to dose. Neither food nor gender affected pharmacokinetics. Tazarotenic acid reached therapeutic levels in skin and was more rapidly eliminated from the systemic circulation than other approved retinoids.

255. Markers of inflammation in brain endothelium after exposure to three forms of amphotericin: potential mechanism of infusion reactions. *Timothy R. McGuire, Pharm.D.*, William J. Trickler, Eric B. Hoie, Pharm.D., Donald W. Miller, Ph.D.; University of Nebraska Medical Center, Omaha, NE.

Common formulations of amphotericin include a deoxycholate colloidal suspension (d-Amph), an amphotericin-B lipid complex (Ablc), and a liposomal product (l-Amph). The clinical incidence of infusion related fever is highest with d-Amph, intermediate with Ablc, and lowest with l-Amph. In the present study, we measured the activation of cyclooxygenase-2 (COX-2) and release of TNF-α and IL-1β from brain microvessel endothelium treated with these three formulations of amphotericin. Primary cultured porcine brain microvessel endothelial cells (PBMEC) were exposed to d-Amph, Ablc and l-Amph at clinically relevant concentrations. Media samples from the cells were collected and analyzed for TNF-α and IL-1β. Release of these cytokines from PBMEC monolayers treated with l-Amph were similar to cells receiving culture media alone. In contrast, Ablc and d-Amph caused significantly greater release of both TNF-α and IL-1β. Contrary to conventional wisdom TNF-α was the initial inflammatory cytokine released with IL-1β being released later. In previously presented data we demonstrated a rise in PgE-2 within 1 hour of treating endothelium with amphotericin. We confirmed by Western blot analysis an induction of COX-2 expression in BPMEC following LPS, Ablc or d-Amph treatment. These studies indicate that amphotericin induces COX-2 expression in brain microvessel endothelium which is responsible for PgE-2 release and fever. TNF-α is released early from endothelium and is more likely than IL-1β to mediate amphotericin induced infusion reactions. The signal transduction pathways involved in amphotericin induced fever are under investigation.

256. Meta-analysis to evaluate factors affecting serum cortisol following fluticasone propionate. *Sharon C. Murray, Ph.D.*, Rashmi S. Mehta, Ph.D., Robert L. Kunka, Ph.D., Shuching Shaw, M.S., Yonghua Wang, Ph.D.; GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: The primary objective of this analysis was to identify covariates that influence serum cortisol levels following fluticasone propionate (FP) administration. Specific hypotheses included the effect of gender.
METHODS: The data used in this meta-analysis comes from 182 subjects in five Phase II/III/IV studies; FLTA2001, FLD230, FLTA3025, FAS40022, and FMS40243. Serum cortisol was used as a measure of the pharmacodynamics (PD) of FP. The effects of the following covariates were investigated on the PD of FP: Demographic data [age, gender, body mass index (BMI), baseline FEV_1, percent predicted FEV_1, disease category (healthy, asthma or COPD)], Dose used in the study (Placebo, 100 µg, 250 µg, 500 µg), and Formulation (Powder, Aerosol). Effects of these covariates were evaluated using ANCOVA with cortisol as the response variable in the model.
RESULTS: Adjusted mean differences (95% CI) in serum cortisol AUC between females and males for the placebo, 100 µg, 250 µg, and 500 µg groups, respectively, were 814.5 (18.0, 1610.9), 697.6 (-1137.7, 2532.8), 979.3 (17.1, 1941.5), and 403.5 (-26.8, 833.8). Gender, formulation and percent predicted FEV_1 had statistically significant effects on serum cortisol ($p=0.0129$, 0.0234 and 0.0472, respectively).
CONCLUSIONS: Meta-analysis showed that cortisol levels are higher in females compared to males. This difference is independent of FP treatment and was also observed after placebo treatment. Serum cortisol levels were also affected by formulation and pulmonary function. Disease category (asthma, COPD, or healthy), age, and body mass index did not affect cortisol.

257E. Cantharidin-induced inflammatory blister technique: focus on healing and blister resolution. *Dana Maglio, Pharm.D.*, Charles H. Nightingale, Ph.D., David P. Nicolau, Pharm.D., FCCP; Hartford Hospital, Hartford, CT.

Presented at the 42nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA, September 27-30, 2002.

258. The pharmacokinetics of pantoprazole and omeprazole in patients with erosive gastroesophageal reflux disease. *Vijaya S. Pratha, M.D.*, Robyn G. Karlstadt, M.D., Richard B. Lynn, M.D., Michael S. Burton, B.S., Daniel L. Hogan, Ph.D.; Clinical Applications Laboratories, San Diego, CA; Wyeth Pharmaceuticals, St. Davids, PA.

PURPOSE: Pharmacokinetics (PK) of pantoprazole and omeprazole are well described in healthy subjects. In a previous study in healthy subjects, pantoprazole 40 mg demonstrated greater acid inhibition than omeprazole 20 mg (Pratha et al. Otolaryngol Head Neck Surg. 2002;in press). The purpose of this study was to characterize the PK of these proton pump inhibitors in patients with erosive gastroesophageal reflux disease (GERD).
METHODS: 35 patients (23 M,12 F) with documented GERD completed this double blind crossover study. Treatment consisted of a 14-day run-in preceding 5 days of daily oral pantoprazole 40 mg or omeprazole 20 mg followed by a 15-day washout. Serial blood samples for PK values were drawn on days 1 and 5 in each active-drug phase.
RESULTS: The mean AUC of pantoprazole was similar on day 1 and day 5 (15.2 and 16.9 µmol•h/L, $p=0.41$) as expected due to its lack of effect on liver enzymes. However, the AUC for omeprazole increased significantly ($p<0.05$) over the 5-day treatment period from 3.0 (day 1) to 4.4 µmol•h/L (day 5). Similarly, mean C_{max} was similar for pantoprazole (7.1 to 8.1 µmol/L; $p=0.12$), but significantly higher on day 5 than day 1 for omeprazole (1.2 to 1.6 µmol/L, $p<0.05$).
CONCLUSIONS: In patients with documented GERD, the significantly ($p<0.01$) higher AUC and C_{max} for pantoprazole, compared with omeprazole, may contribute to greater inhibition of proton pumps activated throughout the day. This prolonged serum drug availability as well as greater acid inhibition as seen in healthy subjects may partially explain why pantoprazole provides nighttime heartburn relief.

259. Oral telithromycin for 7 to 10 days is as effective as standard comparators for the treatment of community-acquired pneumonia. *John Pullman, M.D.,* Bruno Leroy, M.D.; Mercury Street Medical, Butte, MT; Aventis Pharmaceuticals, Bridgewater, NJ.

Hypothesis: Telithromycin, a ketolide antibacterial, is equivalent to standard comparators in the treatment of community-acquired pneumonia (CAP), including infections caused by atypical/intracellular pathogens.
METHODS: The efficacy of telithromycin 800 mg QD for 7 to 10 days in 503 adult patients with symptoms of CAP (radiologically confirmed) and stratified according to Fine score, was assessed in three randomized, double-blind, multicenter Phase III studies. Comparator groups (n=521) received either amoxicillin 1000 mg TID or clarithromycin 500 mg BID for 10 days, or trovafloxacin 200 mg QD for 7 to 10 days.
RESULTS: The clinical cure rate for telithromycin post-therapy (Days 17 to 24) was 91.0% (356/391) in the per-protocol (PPc) population vs. 90.4% (356/394) for pooled comparators. In patients at increased risk of morbidity and mortality, clinical cure with telithromycin vs. comparators was 91.8% (56/61) vs. 83.3% (65/78) in those with a Fine score ≥III, 88.3% (53/60) vs. 84.8% (56/66) in subjects aged ≥65, and 93.8% (15/16) vs. 84.6% (11/13) in patients with pneumococcal bacteremia. Among the PPc group for whom a pretreatment causative pathogen was identified, bacteriologic outcome was satisfactory in 90.2% (74/82) of telithromycin-treated patients compared with 93.3% (84/90) of comparator-treated patients. Clinical cure rates for patients infected with atypical/intracellular pathogens were 90.0% (198/220) of the telithromycin group vs. 88.3% (181/205) of comparator groups.
CONCLUSIONS: Telithromycin 800 mg once daily for 7 to 10 days offers a convenient first-line therapy, equivalent to comparators, for empiric treatment of CAP, providing high rates of clinical and bacteriologic efficacy.

260. Effect of high-fat breakfast and moderate-fat evening meal on the pharmacokinetics of vardenafil, a potent, highly selective PDE-5 inhibitor for the treatment of erectile dysfunction. *Prabhu Rajagopalan, Ph.D.,* Arthur Mazzu, Ph.D., Chenghua Xia, Ph.D., Ray Dawkins, M.D., Pavur Sundaresan, M.D., Ph.D.; Bayer Corporation, West Haven, CT; PDD Development, Morrisville, NC.

PURPOSE: To assess the effects of a high-fat breakfast and a typical moderate-fat evening meal on the pharmacokinetics of vardenafil.
METHODS: In this randomized crossover study, vardenafil 20 mg was administered to 25 healthy males (mean age 29 years, mean BMI 25 kg/m^2) at 8AM after an overnight fast or immediately after consumption of a high-fat breakfast (57% fat), at 6 PM on an empty stomach or after consumption of a moderate-fat meal (30% fat). Blood samples were analyzed for vardenafil and metabolite M1 levels; pharmacokinetic parameters were determined using non-compartmental methods.
RESULTS: High and moderate fat meals did not alter vardenafil pharmacokinetic parameters [geometric mean (%CV) shown in Table] to clinically significant degree. Moderate-fat meal did not alter T_{max} and high-fat meal delayed median T_{max} by an hour.

	AM			PM		
	Fasting (n = 22)	High-fat breakfast (n = 22)	Geometric LS mean ratio[A] (90% CI)	Fasting (n = 24)	Moderate-fat meal (n = 24)	Geometric LS mean ratio[B] (90% CI)
C_{max}, µg/L	17.14 (65)	14.00 (68)	0.82 (0.67-1.00)	14.22 (70)	13.04 (66)	0.92 (0.76-1.11)
T_{max}, h[C]	1.0 [0.5-2.5]	2.0 [0.5-4.0]	—	1.0 [0.5-3.0]	1.0 [0.5-4.0]	—
AUC, µg•h/L	66.78 (67)	67.09 (59)	1.01 (0.87-1.17)	51.97 (72)	59.12 (56)	1.14 (0.99-1.31)
Half-life, h	3.3 (50)	3.3 (41)	0.99 (0.79-1.24)	3.9 (66)	3.8 (39)	0.97 (0.79-1.20)

[A]High-fat breakfast/AM fasting; [B]Moderate-fat meal/PM fasting; [C]Median [range]

A similar observation was made for metabolite M1. Treatments were well tolerated. No serious adverse events were reported. Headache (most common event) was reported in 1-3 subjects per treatment.
CONCLUSION: Vardenafil pharmacokinetics are largely unaffected by food containing high or moderate amounts of fat.

261E. Pharmacokinetics and metabolism of transdermally administered oxybutynin. R.H. Zobrist, Ph.D., H.M. Thomas, Ph.D., *S.W. Sanders, Pharm.D.*; Watson Laboratories, Inc., Salt Lake City, UT.

Presented at the Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, Atlanta, GA, March 24-27, 2002.

262E. Population pharmacokinetics of transdermally administered oxybutynin. *S.W. Sanders, Pharm.D.*, H.M. Thomas, Ph.D., R.H. Zobrist, Ph.D.; Watson Laboratories, Inc., Salt Lake City, UT.

PURPOSE: Population pharmacokinetics of oxybutynin (OXY) and its active metabolite, N-desethyloxybutynin (DEO), during 24 weeks of transdermal OXY treatment of patients with overactive bladder.
METHODS: Following IRB approval and written informed consent, 520 adult patients participated in a 12-week randomized, double-blind, placebo-controlled evaluation of the efficacy and safety of transdermal OXY followed by 12 weeks of open-label treatment. Population pharmacokinetics were evaluated based on samples collected during treatment. Plasma samples were measured by a validated LC/MS method with CV < 10%.
RESULTSPlasma concentrations of OXY and DEO varied in proportion to nominal delivered dose and were consistent with previous studies in healthy volunteers. Patient age, weight, gender, race, tobacco use, and concurrent illness were not associated with differences in plasma OXY and DEO concentrations. Withdrawals due to application site reactions occurred in 4.8% of patients; dry mouth was reported by 9.6% of patients in the 3.9 mg/d dosing group.
Mean (SD) Plasma Oxybutynin and DEO Concentrations (ng/mL) by Dose and Treatment Duration

	OXY			DEO		
	Week 6	Week 12	Week 24	Week 6	Week 12	Week 24
1.3 mg/day Treatment Group						
N	115	104	33	114	104	33
Mean (SD)	1.18 (0.54)	1.24 (0.62)	1.17 (0.75)	2.10 (1.38)	2.19 (1.64)	1.83 (1.33)
DEO:OXY	1.7	1.8	1.7	—	—	—
2.6 mg/day Treatment Group						
N	117	103	113	117	102	113
Mean (SD)	2.55 (1.42)	2.62 (1.38)	2.51 (1.54)	4.37 (3.21)	4.25 (2.95)	4.41 (3.37)
DEO:OXY	1.7	1.6	1.7	—	—	—
3.9 mg/day Treatment Group						
N	110	100	180	110	100	180
Mean (SD)	4.08 (2.10)	3.69 (1.88)	3.80 (2.21)	7.88 (6.37)	6.47 (4.08)	6.67 (5.51)
DEO:OXY	1.9	1.8	1.7	—	—	—

CONCLUSIONS: Transdermal delivery of OXY avoids presystemic gastrointestinal and hepatic metabolism. Reproducible plasma concentrations are observed during chronic treatment due to consistent transdermal delivery and dose-independent metabolism and disposition. Transdermal OXY is a convenient and well-tolerated route of administration that improves OXY therapeutic index.
Presented at the Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, Atlanta, GA, March 24-27, 2002.

263. Ximelagatran, an oral direct thrombin inhibitor, normalizes platelet activation and inhibits thrombin generation in patients with non-valvular atrial fibrillation. Michael Wolzt, M.D., Stig-L Bostrom, Ph.D., Maria Wollbratt, M.Sc., Mia Svensson, M.Sc., Ulf G. Eriksson, Ph.D., Margaretha Grind, M.D., Ph.D., *Troy C. Sarich, Ph.D.*; University of Vienna, Vienna, Austria; AstraZeneca R&D, Molndal, Sweden; AstraZeneca R&D, Loughborough, United Kingdom; AstraZeneca LP, Wilmington, DE.

PURPOSE: To investigate the pharmacodynamics of melagatran, the active form of ximelagatran, on platelet activation and thrombin generation in patients with non-valvular atrial fibrillation (NVAF) and healthy subjects.
METHODS: In this open, nonrandomized study, 12 NVAF patients with low risk of thromboembolism and 12 healthy age- and sex-matched control subjects received a 10 minute 2.66 mg iv melagatran infusion on Day 1 followed by 36 mg BID oral ximelagatran for 5 subsequent days. Platelet expression of P-selectin (%) and endogenous thrombin potential (ETP) were assessed from blood samples at pre-entry, Day 1 (pre-iv melagatran), and Day 6 (2 hours post-oral ximelagatran).
RESULTS: Day 1 P-selectin expression was 45% higher in NVAF patients (INR≤2.0) compared with controls (estimated mean difference: 3.41, 95% CI: 0.59, 6.24). On Day 6, this difference was no longer detectable (estimated mean difference: 2.14, 95% CI: –0.47, 4.75). Pre-entry ETP area under the plasma concentration-vs.-time curve (AUC; i.e., during VKA/warfarin therapy) was significantly lower in NVAF patients than controls (estimated mean difference: –680 nM•min, 95% CI: –1235, –125). Ximelagatran treatment reduced ETP-AUC in both patients and controls (estimated mean differences between Days 1 and 6: –495 nM•min, 95% CI: –747, –242 and –491 nM•min, 95% CI: –739, –243, respectively). Time to peak thrombin generation was increased in NVAF patients and controls (estimated mean differences between Days 1 and 6: 2.21 min, 95% CI: 0.76, 3.67 and 1.2 min, 95% CI: 0.43, 1.97, respectively).
CONCLUSION: Direct thrombin inhibition with ximelagatran normalized P-selectin expression and inhibits and delays thrombin generation.

264. Comparative effects of celecoxib and rofecoxib on COX-1 and COX-2 activity in whole blood assays. *Jules I. Schwartz, Pharm.D., M.P.H.*, Arturo G. Porras, Ph.D., Peggy H. Wong, Ph.D., Anne Van Hecken, Ph.D., Inge De Lepeleire, Pharm.D., Aimee Dallob, M.S., Thomas Hunt, M.D., Ph.D., David L. Ebel, B.S., Carol P. Gumbs, B.S., Keith Gottesdiener, M.D., Barry J. Gertz, M.D., Ph.D., Paul J. De Schepper, M.D., Ph.D.; Merck and Co, Inc., Rahway, NJ; Merck and Co, Inc., Brussels, BE; Merck and Co, Inc., West Point, PA; Catholic University, Leuven, Belgium; PPD, Inc., Austin, TX.

PURPOSE: This study compares the COX-1 and COX-2 activities in whole blood assays between different regimens of rofecoxib and celecoxib, which were not previously compared directly.
METHODS: Healthy subjects (N = 97) (18-75 years) were evaluated in 2 similar double-blind, randomized, placebo-controlled, parallel-group trials where rofecoxib 12.5 mg QD, 25 mg QD, 50 mg QD, celecoxib 200 mg QD,

celecoxib 200 mg BID, or placebo were administered for 7 days. Blood was taken for whole-blood assays of COX-2 (ex vivo LPS induced PGE_2) and COX-1 (ex vivo generated serum TXB_2) activities and plasma drug concentrations on Day 7 predose and at selected time points over the 24 hours post dose. Pharmacodynamic and pharmacokinetic data were pooled across studies to assess the relationship between COX-1 and COX-2 activities and drug plasma concentrations.
RESULTS:

Treatment	N	Percent Inhibition of COX-2 Activity from Day 1 Baseline (mean ± SE)† Average Over Dosing Interval	At Trough
Placebo	26	2.73 (3.88)	8.55 (5.24)
Rofecoxib 12.5 mg QD	12	37.14 (4.61)	28.54 (5.29)
Rofecoxib 25 mg QD	12	64.45 (2.56)	58.54 (1.77)
Rofecoxib 50 mg QD	16	76.62 (2.64)	71.87 (3.31)
Celecoxib 200 mg QD	16	46.91 (4.58)	10.44 (14.26)
Celecoxib 200 mg BID	15	64.63 (2.99)	63.24 (3.93)

†Ex Vivo LPS Stimulated PGE_2

Inhibition of COX-2 activity increased with increasing plasma concentrations of rofecoxib or celecoxib. There was no clinically important inhibition of COX-1 activity for either drug.
CONCLUSIONS: Rofecoxib 25 mg QD and celecoxib 200 mg BID have similar inhibitory effects on COX-1 and COX-2 activity.

265. Pharmacokinetic variability in patients receiving large dose-extended interval aminoglycosides. *Jennifer M. Sickels, Pharm.D.,* Maryann Hawes, Pharm.D. candidate; Northeastern University, Boston, MA.

PURPOSE: Administering large dose-extended interval (LDEI) aminoglycosides to patients with variable pharmacokinetics could result in prolonged drug-free periods resulting in decreased efficacy. The purpose of this study was to identify characteristics and evaluate clinical outcomes of patients who received LDEI aminoglycosides and had low random serum concentrations.
METHODS: Medical records of patients who received LDEI aminoglycosides from 8/95-3/01 were reviewed. Patients with random concentrations ≤ 2 mg/dL (within 12 hours post-dose) were enrolled in the study group; patients with random concentrations > 2 mg/dL were enrolled in the control group. Demographic data, factors that could affect pharmacokinetics, and clinical outcomes were documented.
RESULTS: A total of 278 patients were evaluated. Compared to controls (n=139), study patients (n=139) were younger (43.39 years vs. 58.71 years, p<0.0001); had better renal function (CrCl 88.34 mL/min vs. 71.39 mL/min, p<0.0001); and lower actual body weight (72.54 kg vs. 78.59 kg, p<0.0001). No association was identified between low random concentrations and critical illness, neutropenia, quadriplegia, or ascites. Clinical cure or improvement rates were similar between groups (85% vs. 91%, p=0.2016). No significant differences were found between groups in rates of dosage changes (39% vs. 30%, p=0.17), duration of therapy (5.25 days vs. 5.88 days, p=0.09), or number of concentrations drawn per patient (1.67 vs. 1.70, p=0.85). Nephrotoxicity was less common in the study group (RR=0.33; 95%CI=0.1627-0.6828).
CONCLUSION: Characteristics associated with low random concentrations included decreased age, increased renal function, and decreased weight. Low random concentrations did not result in decreased efficacy in our study population.

266E. An in vitro study of the administration of esomeprazole enteric-coated pellets through naso-gastric and gastromy tubes. *Mark B. Sostek,* Eva Blychert, Anders Karlsson, Anna Hulthe; AstraZeneca LP, Wayne, PA; AstraZeneca R&D Molndal, Molndal, Sweden.

Presented at the 67th Annual Meeting of the American College of Gastroenterology, Seattle, WA, October 18-23, 2002.

267. Effect of sex on the pharmacokinetics of ciprofloxacin. *Brian R. Overholser, Pharm.D.,* Michael B. Kays, Pharm.D., Kevin M. Sowinski, Pharm.D.; Purdue University; Indiana University, Indianapolis, IN.

Two previous studies showed no differences in oral ciprofloxacin pharmacokinetics between males and females.
PURPOSE: To assess the influence of sex on the pharmacokinetics of oral ciprofloxacin.
METHODS: Fifteen healthy subjects (8 males, 7 females) were enrolled. They were admitted to the research unit in the morning of the study day and were required to fast ≥ 8 hour prior to admission. Each subject received a single oral dose of ciprofloxacin 750 mg. Serial blood samples were collected immediately before and 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hour after administration. Ciprofloxacin serum concentrations were determined by HPLC, and pharmacokinetic models were fitted to the data using ADAPT II software. Initially, models were fit to the data with a weighted (inverse of observation variance) least squares estimator. These estimated parameters were used to compute maximum a posteriori Bayesian priors, and the data were reanalyzed using the maximum a posteriori procedure. In all subjects, a two-compartment open-model with two parallel first-order inputs and elimination from the central compartment was chosen as the model of best-fit by Akaike's Information Criterion and visual inspection. Differences in pharmacokinetic parameters between males and females were determined using the Student's t-test.
RESULTS: The average ages of males and females were not significantly different, 31.8 ± 6.4 vs. 28.0 ± 5.3 years. The average weights were 87.2 ± 14.1 and 58.4 ± 7.3 kg (p<0.05) for males and females, respectively. Estimated pharmacokinetic parameters and calculated secondary parameters (mean ± SD) are shown in the table below.

	Cl_s/F (L/hour)	Cl_s/F (L/hour/kg)	Cl_d (L/hr)	V_c/F (L)	V_p/F (L)
Males	45.8 ± 4.4*	0.54 ± 0.09	27.2 ± 16.2	90.2 ± 22.7	101 ± 31.9*
Females	29.3 ± 3.9	0.51 ± 0.08	17.8 ± 15.0	88.2 ± 10.1	49.2 ± 11.8

(continued)

	V_{ss}/F (L)	V_{ss}/F (L/kg)	$t_{1/2}$ (hr)	C_{max} (µg/ml)
Males	191 ± 28*	2.23 ± 0.42	5.41 ± 1.62	3.16 ± 0.86*
Females	137 ± 17	2.36 ± 0.14	4.90 ± 1.28	4.45 ± 0.66

*p<0.05

CONCLUSIONS: Differences exist in ciprofloxacin pharmacokinetics between males and females due to differences in body weight. Fixed doses of ciprofloxacin given without regard to body weight will lead to higher drug exposure in females compared to males.

268. Herbal teas and their effect on hepatic drug metabolizing enzymes in rats. *Sompon Wanwimolruk, Ph.D.,* Pius P. Maliakal, Ph.D.; Western University of Health Sciences, Pomona, CA; University of Otago, Dunedin, New Zealand.

PURPOSE: The present study was conducted to determine the effect of herbal teas (Peppermint, Chamomile and Dandelion tea) on the activity of hepatic phase I and phase II metabolizing enzymes using rat liver microsomes.
METHODS: Female Wistar rats were divided into 6 groups (n = 5 each). Three groups had free access to tea solutions (2%) while the control group had water. Two groups received either green tea extract (0.1%) or aqueous caffeine solution (0.0625%). After 4 weeks of pretreatment, different cytochrome P450 (CYP) isoforms and phase II enzyme activities were determined by incubation of liver microsomes or cytosols with appropriate substrates.
RESULTS: Activity of CYP1A2 in liver microsomes of rats receiving Dandelion, Peppermint and Chamomile tea were significantly decreased ($p < 0.05$) to 15%, 24% and 39% of the control value, respectively. CYP1A2 activity was significantly increased by pretreatment with caffeine solution. No alterations were observed in the activities of CYP2D and CYP3A in any groups of pretreated rats. Activity of CYP2E in rats receiving Dandelion and Peppermint tea was significantly lower ($p < 0.05$) than in the control group, i.e. 48% and 60% of the control. There was a dramatic increase (244% of control) in the activity of phase II detoxifying enzyme UDP-glucuronosyl transferase in Dandelion tea pretreated group. There was no change in the activity of glutathione-S-transferase.
CONCLUSION: The results suggest that like green and black teas, certain herbal teas can cause modulation of phase I and phase II drug metabolizing enzymes.

269E. Pharmacokinetic comparison of five proton pump inhibitors. *Lynda S. Welage, Pharm.D.,* Robyn G. Karlstadt, M.D., Michael S. Burton, B.S., Richard B. Lynn, M.D.; University of Michigan, Ann Arbor, MI; Wyeth-Ayerst Pharmaceuticals, St. Davids, PA.

Presented at the Annual Meeting of Digestive Disease Week, San Francisco, CA, May 19, 2002.

270. Effect of multiple-dose olanzapine on the steady-state pharmacokinetics of valproic acid in patients with bipolar or schizoaffective disorder. *Heidi S. Wirtz, Pharm.D.,* Robert W. Baker, M.D., Richard F. Bergstrom, Ph.D.; Lilly Corporate Center, Indianapolis, IN.

PURPOSE: This study examines whether olanzapine co-therapy with lithium or valproate reduces symptomatic recurrence compared to lithium or valproate monotherapy in patients suffering from bipolar disorder.
METHODS: Patients who were in syndromic remission of bipolar disorder after 6 weeks of acute therapy with olanzapine plus lithium (0.6–1.2 mEq/L) or valproate (50–125 µg/mL) were randomized to receive olanzapine (5–20 mg/day) or placebo with continued co-therapy for 18 months of double-blind therapy.
RESULTS: Among patients who were symptomatic remission of mania (Y-MRS ≤12) the olanzapine treated-treated patients (n=46) had a significantly longer time to recurrence into mania than monotherapy-treated patients (n=48; estimated 25th percentile: 362 vs. 63 days, respectively; P=0.005). Rates of recurrence into mania also significantly favored olanzapine-treated patients (monotherapy, 35.4% vs. olanzapine, 15.2%; P=0.033). Recurrence into depression was evaluated in a set of patients who were in symptomatic remission of mania and depression (HAMD-21 ≤ 8) following acute therapy. Time to and rates of recurrence into depression were not significantly different between treated (n=30) and monotherapy (n=38) groups, but were numerically favorable for the olanzapine treated group (155 vs. 27 days,

respectively; p=0.071; 23.3% vs. 39.5%, respectively; p=0.197). Importantly, time to recurrence to either pole significantly favored the olanzapine co-therapy group (25th percentile: olanzapine co-therapy, 124 days; monotherapy, 15 days, p=0.023).
CONCLUSIONS: The results suggest that the combination of olanzapine plus lithium or valproate effectively prolonged time in remission in comparison to lithium or valproate monotherapy.

271. Telithromycin is as effective as standard comparators in the treatment of community-acquired respiratory tract infections. *Marcus Zervos, M.D.,* James T. Hawa, D.O.; William Beaumont Hospital, Royal Oak, MI; Benbrook Family Practice, Benbrook, TX.

HYPOTHESIS: telithromycin (TEL), a ketolide antibacterial, is equivalent to standard comparators (CMPs) in the treatment of community-acquired respiratory tract infections.
METHODS: In seven Phase III randomized, double-blind, active-controlled trials, patients with community-acquired pneumonia (CAP), acute exacerbation of chronic bronchitis (AECB), and acute maxillary sinusitis (AMS) were treated with TEL or CMPs. CAP: In three studies, subjects received 7 to 10-day TEL 800-mg QD, 10-day amoxicillin 1000-mg TID, 10-day clarithromycin 500-mg BID, or 7 to 10-day trovafloxacin 200 mg QD. AECB: In 2 studies, subjects received 5-day TEL 800-mg QD, or 10-day amoxicillin/clavulanate (A/C) 500/125-mg TID or cefuroxime axetil (CEF) 500-mg BID. AMS: In two studies, subjects received 5- or 10-day TEL 800-mg QD, or 10-day A/C 500/125-mg TID or CEF 250-mg BID.
RESULTS: In the pooled, modified, intent-to-treat population (N=2680), 1490 patients received TEL, 1190 CMPs. At post-therapy/test-of-cure (Days 17 to 24), TEL and CMP achieved comparable clinical cure rates in per-protocol patients with CAP (91.0% TEL vs. 90.4% CMP), AECB (86.3% TEL vs. 82.7% CMP), and AMS (78.5% TEL vs. 77.4% CMP). Similar clinical cure rates at late post-therapy (Days 31 to 45) were also seen with TEL compared with CMP in treating CAP (88.3% TEL vs. 86.8% CMP), AECB (78.4% TEL vs. 75.8% CMP), and AMS (73.1% TEL vs. 73.6% CMP). Telithromycin also achieved high rates of bacterial eradication.
CONCLUSIONS: Once-daily TEL achieves clinical cure rates equivalent to CMPs in treating community-acquired respiratory tract infections.

Pharmacy Practice

272. A comparison of the responsibilities of tenure versus non-tenure track pharmacy practice faculty. *Mark L. Glover, Pharm.D.,* Lisa Deziel-Evans, Pharm.D., Ph.D.; Nova Southeastern University, Ft. Lauderdale, FL.

PURPOSE: To determine if tenure and non-tenure track pharmacy practice faculty differ with respect to their involvement with teaching, research, and service activities.
METHODS: A survey identifying the teaching, research, and service activities of faculty was mailed to the respective chair within the division of pharmacy practice of 82 United States Schools of Pharmacy. Responses to each of the survey questions were compared between tenure and non-tenure faculty and between those schools who employ both tenure and non-tenure track faculty. Comparisons included: 1) the number of weeks per year precepting students, 2) the number of clerkship students precepted per year, 3) the number of didactic hours taught per year, 4) the number of peer-reviewed articles published per year, and 5) the number of committee assignments per year.
RESULTS: A total of 71 (87%) surveys were returned with two being excluded due to incomplete data. Of the 69 pharmacy practice departments represented, analysis of all responses indicated tenure track faculty publish more articles per year (1.5 vs. 0.6) and serve on more committees (2.1 vs. 1.8) while non-tenure track faculty precept more students per year (16.8 vs. 13) and for more weeks during the year (33.4 vs. 27.6). There was no significant difference regarding the number of didactic hours taught per year between tenure and non-tenure track faculty (36.1 vs. 29.2). Those departments that employ both tenure and non-tenure track faculty indicated a significant difference between the two groups for all questions.
CONCLUSION: Tenure and non-tenure pharmacy practice faculty differ in terms of their required teaching, research, and service activities.

273. Clinical pharmacist staffing in United States hospitals. *C.A. Bond, Pharm.D., FASHP, FCCP,* Cynthia L. Raehl, Pharm.D., FASHP, FCCP, Todd Franke, Ph.D.; Texas Tech University Health Sciences Center, Amarillo, TX.

This study evaluated hospital demographics (census regions, size, teaching affiliation, hospital ownership, hospital pharmacy director's degree, and pharmacist location within the hospital) and clinical pharmacist staffing/occupied beds in United States hospitals. A database was constructed from the 1992 American Hospital Association's Abridged Guide to the Health Care Field and the 1992 National Clinical Pharmacy Services Database. Simple statistical tests and a multiple regression analysis were employed. The study population consisted of 1391 hospitals that reported information on clinical pharmacist staffing. The mean number of clinical pharmacists/occupied bed was 0.51 clinical pharmacists/100 occupied bed.
Factors associated increased clinical pharmacist staffing/occupied bed were West North Central region (slope = 0.0029439, p=0.002), Pacific region (slope = 0.0032089, p=0.004), hospitals affiliated with a pharmacy teaching program (slope = 0.0025330, p=0.0001), teaching hospitals (slope = 0.0028122, p=0.001), federal government hospitals (slope = 0.0029697, p=0.012), directors with the Pharm.D. degree (slope = 0.0335020, p=0.002), directors with the M.S. Pharmacy degree (slope = 0.003), pharmacists in a decentralized location (slope = 0.0035393, p=0.0001), and pharmacy technician staffing (slope = 0.0517713, p=0.0001). Statistically significant associations between demographic variables and decreased clinical pharmacist staffing/occupied bed were Mid-Atlantic region (slope = -0.0028237, p=0.002), small hospitals (slope = -0.0028894, p=0.001; p=0.023), and hospital pharmacy administrator staffing (slope = -0.0184513, p=0.042). Significant differences were observed between clinical pharmacists staffing and hospital demographic factors. These findings will help future researchers in determining the specific reasons why some types of hospitals have higher (and lower) levels of clinical pharmacist staffing.

274. The effect of levofloxacin coadministration on international normalized ratio monitoring of warfarin therapy. *Weeranuj Yamreudeewong, Pharm.D., BCPS, CACP,* Dennis L. Lower, M.D., David M. Kilpatrick, M.D., Ann M. Enlow, F.N.P., Margo M. Burrows, F.N.P.; Cheyenne Veterans Affairs Medical Center, Cheyenne, WY.

PURPOSE: To evaluate the effect of levofloxacin coadministration on international normalized ratio (INR) monitoring in patients receiving warfarin therapy.
METHODS: A total of eighteen patients who were receiving stable doses of warfarin therapy participated in this study. Levofloxacin was prescribed for treatment of different types of infection in these patients based on appropriate diagnoses of the health care providers. The study began after obtaining written informed consent form from the patient. The INR values of each patient were measured before and after levofloxacin initiation. Each study patient was asked to return to the clinic twice weekly for INR monitoring during levofloxacin coadministration. The INR values were also measured after the completion of levofloxacin therapy. Dosages of other concurrent medications that might interact with warfarin were kept constant during the study period. Each patient was asked if any adverse effects had occurred at each clinic visit. After levofloxacin initiation, warfarin doses were adjusted as necessary in patients with the first INR values that were higher or lower than therapeutic ranges.
RESULTS: In some patients, warfarin doses were changed after the first nontherapeutic INR values post levofloxacin administration, therefore only the INR values before and the first INR values after starting levofloxacin therapy were compared. Using the two-tailed paired t-test statistical analysis, results of this study revealed no significant difference in INR values before and after levofloxacin coadministration (P=0.42).
CONCLUSION: The results of this study revealed no significant effect of levofloxacin coadministration on INR monitoring of warfarin therapy.

Psychiatry

275. Randomized trial of pharmacist intervention to improve depression care and outcomes in primary care. *Kam L. Capoccia, Pharm.D.,* Denise M. Boudreau, M.S., Ph.D. candidate, Sean D. Sullivan, Ph.D., David K. Blough, Ph.D., Allan J. Ellsworth, Pharm.D., Dave L. Clark, Pharm.D., Wayne J. Katon, M.D., Edward A. Walker, M.D., Nancy G. Stevens, M.D. MPH; University of Washington, Seattle, WA; Kaiser Permanente, Denver, CO.

PURPOSE: To evaluate the impact of pharmacist intervention to improve depression care and outcomes in primary care.
METHODS: Pragmatic, 1-year trial of a pharmacist collaborative care intervention versus usual care in a family practice clinic. Patients diagnosed with a new episode of major depression and started on antidepressant medications were randomized to enhanced care (EC) or usual care (UC). EC consisted of a pharmacist collaborating with primary care providers to facilitate education, initiation and titration of antidepressant medication, monitor adherence, manage adverse reactions and prevent relapse. Control patients received UC. Outcomes were the Hopkins Symptom Checklist (SCL-20), the DSM-IV criteria for major depression (SCID), health-related quality of life (SF-12), medication adherence, patient satisfaction, and use of depression-related health care services. Intent-to-treat analysis was used.
RESULTS: Seventy-four patients were randomized to EC or UC. At baseline, the EC group was significantly worse than UC based on diagnostic scores (SCID). All analyses were adjusted for this difference. In both groups, mean scores significantly improved for symptoms of depression and quality of life at 3 months and were maintained through one year. There were no statistically significant differences between treatment groups in medication adherence, provider visits and patient satisfaction. Possible explanations for the lack of difference include the consistent availability of six mental health providers in the clinic and the existence of an established role for the pharmacist in usual care.
CONCLUSION: Pharmacist intervention and usual care resulted in dramatic improvements in the outcomes of depression at one year, although not statistically different.

276E. Olanzapine reduction of neuroleptic-induced hyperprolactinemia in schizophrenia. Bruce J. Kinon, M.D., Jonna Ahl, Ph.D., Hong Liu, Ph.D., *Virginia L. Stauffer, Pharm.D.*; Eli Lilly & Company, Indianapolis, IN.

Presented at the Annual Meeting of the Society of Biological Psychiatry, Philadelphia, PA, May 16, 2002.

277E. Olanzapine and olanzapine-fluoxetine combination in the treatment of bipolar depression. Mauricio Tohen, M.D., Ph.D., Eduard Vieta, M.D., Ph.D., Terence Ketter, M.D., Franca Centorino, M.D., Joseph Calabrese, M.D., Gary Sachs, M.D., Charles Bowden, M.D., Richard Risser, M.S., Robert W. Baker, M.D., Angela R. Evans, Ph.D., *Virginia L. Stauffer, Pharm.D.*, Sanjay Dube, M.D., Gary Tollefson, M.D., Ph.D., Alan Breier, M.D.; Eli Lilly & Company; Indianapolis, IN; Harvard Medical School/McLean Hospital, Belmont, MA; IDIBAPS, Barcelona, Spain; Stanford University, Stanford, CA; Case Western Reserve University; Cleveland, OH; University of Texas Health Sciences Center, San Antonio, TX.

Presented at the International Conference of the American Psychiatric Association, Philadelphia, PA, May 18, 2002.

278. Prescribing patterns of atypical antipsychotics among primary care and non-primary care physicians. *Janet L. Ramsey M.S.*, Allen W. Nyhuis M.S., Danielle L. Loosbrock, M.H.A., Robert A. Browne, M.D.; Eli Lilly & Company, Indianapolis, IN.

PURPOSE: The purpose of this study was to examine the prescribing patterns of commonly used atypical antipsychotics by physician type and patient age group.
METHODS: From 1998 to 2001, a total of 5,697 prescriptions were written for olanzapine (n=2429), quetiapine (n=747), and risperidone (n=2521) in the National Disease and Therapeutic Index™ database. Physician specialty type was categorized into two groups: primary care physicians (PCP), which included Internal, Family, Osteopathic and General Medicine, Geriatrics and Pediatrics), and non-primary care physicians (non-PCP), which included Psychiatry and other specialists. Patient age was divided into three categories: Child/Adolescent (age 0-19), Adult (age 20-59), and Geriatric (age 60 and above).
RESULTS: Across atypical antipsychotics, 83.8% of all prescriptions were written by non-PCPs (mostly psychiatrists). One-quarter (25.3%) of all atypical antipsychotic prescriptions were for geriatric individuals, while 60.2% and 14.5% were written for Adult and Child/Adolescent patients, respectively. Risperidone was the most commonly prescribed agent for Child/Adolescent patients, representing 62.8% of all Child/Adolescent prescriptions. Nearly half (47.5%) of atypical antipsychotic prescriptions written by PCPs were for the Geriatric population. Of the Geriatric prescriptions, a significantly larger proportion of risperidone prescriptions (36.8%) were written by PCPs versus non-PCPs than olanzapine (26.9%; $p<0.001$) or quetiapine (13.4%; $p<0.0001$).
CONCLUSIONS: Across physician specialty, differences exist in prescribing patterns for atypical antipsychotics particularly within Geriatric and Child/Adolescent populations. Further research is needed to examine the reasons for the atypical antipsychotic prescribing differences between PCP and non-PCPs.

279. The effects of ethnicity and antipsychotic type on medication adherence in a Medicaid population. *Jayme L. Opolka, M.S.*, Karen L. Rascati, Ph.D., Carolyn M. Brown, Ph.D., P. Joseph Gibson, Ph.D.; University of Texas at Austin, Austin, TX; Eli Lilly & Company, Indianapolis, IN.

PURPOSE: Clinicians treating schizophrenia face increasingly diverse populations. Different ethnic groups have different approaches to medication adherence. The purpose of this study was to examine the association between antipsychotic medication adherence and ethnicity or the specific medication used, after controlling for other factors.
METHODS: Texas Medicaid claims were retrieved for persons, age 21 to 65, diagnosed with schizophrenia or schizoaffective disorder, initiating treatment with olanzapine (n = 1875), risperidone (n = 982), or haloperidol (n = 726) between 1/1997 and 8/1998. For each of the three pairings of these medications, the association between ethnicity (African American, Mexican American, or White) or medication and days use of the medication in the year following initiation was assessed using multivariate linear regression. Covariates included other patient demographics, region, comorbid health conditions, and prior medication and heath care resource use.
RESULTS: Overall mean adherence was 177 of 365 days (48.5%). African Americans and Mexican Americans were significantly less adherent than Whites in the haloperidol versus olanzapine and risperidone versus olanzapine comparisons ($p<0.05$ for each comparison). For patients of all ethnicities, olanzapine was associated with 19 more adherent days than risperidone and 56 more adherent days than haloperidol ($p<0.001$ for each pair-wise comparison).
CONCLUSION: When other factors were controlled for 1) ethnicity was a significant predictor of adherence following initiation on an antipsychotic medication and 2) patients of all ethnicities were most adherent when taking olanzapine, less adherent when taking risperidone, and least adherent when taking haloperidol.

280. The targeted utilization of serotonin-specific reuptake inhibitors within a large managed care organization. *Jamie Daugherty Andrews, Pharm.D.*, Shirley J. Reitz, Pharm.D., BCPS, James A. Carlson, Pharm.D., Sunshine D. Sommers, M.S., R.Ph.; University of Washington, Seattle, WA.

PURPOSE: This initiative was designed to promote the selection of fluoxetine as the SSRI of choice in patients new to SSRI therapy at Group Health Cooperative. This report examines 1) success of the initiative in establishing fluoxetine as first-line therapy 2) maintenance of new patients on fluoxetine over time.
METHODS: Educational efforts including newsletters, electronic communications, and academic detailing were begun to support the initiative. Prescription data was then examined monthly to determine percentage of SSRI new starts on fluoxetine and maintenance of these patients on fluoxetine. Monthly reports were developed to provide continual feedback on compliance with the initiative at various levels, including providers.
RESULTS: 1) Fluoxetine was prescribed in 17% of patients new to SSRI therapy before the initiative began. It was prescribed as follows after introduction of the initiative: January- 49%; February- 55%; March- 62%; April- 67%; May- 72%. 2) As of May 31, 67% (n=1684) of patients started on fluoxetine since January 1 had received another SSRI prescription. 89% of those patients continued on fluoxetine; 5% subsequently received paroxetine; 4% sertraline, and 2% citalopram.
CONCLUSION: Despite initial resistance based on unestablished mythology that fluoxetine is less well-tolerated than other SSRIs, the Fluoxetine First Initiative has been very successful in establishing fluoxetine as SSRI of choice without adding formulary restrictions on other SSRIs. Furthermore, the great majority of patients who were started on fluoxetine have continued on fluoxetine. These continuation rates do not differ from that of the other SSRIs within our organization.

281. An open trial of quetiapine for aggression in children and adolescents with attention deficit hyperactivity disorder. *William A. Kehoe, Pharm.D., M.A.*, Robert B. Schorr, D.O.; University of the Pacific, Stockton, CA; Psychiatric Medical Group, Modesto, CA.

PURPOSE: Aggression is common in children with ADHD. Psychostimulants often do not provide adequate treatment, and antipsychotics have been used. This study evaluated the impact on aggression of the addition of quetiapine to psychostimulants.
METHODS: Ten children and adolescents aged 6-14 years with ADHD and aggression that inadequately responded to a psychostimulant were given quetiapine in an open, uncontrolled, prospective trial. The initial dose was 25 mg q HS and titrated as tolerated to a maximum of 200 mg per day. The primary outcome variable was the change in the "aggression" score on the Child Behavior Checklist (CBCL) after a minimum of 4 weeks of treatment. Secondary outcomes included changes in the "externalizing" and "internalizing" scores on the CBCL. Data were analyzed using two-tailed t-tests. Side effects were monitored using the Treatment Emergent Side Effects Scale.
RESULTS: The addition of quetiapine to psychostimulant therapy resulted in significant reductions in aggression scores (25%, $p=0.033$). Externalizing behaviors (aggression and delinquency) were significantly reduced (27%, $p=0.015$). Internalizing behaviors (withdrawn, social and attention problems) were also significantly reduced (23%, $p= 0.012$). No serious side effects requiring discontinuation of therapy were observed. The most common ones included sedation and fatigue observed in 3 patients.
CONCLUSIONS: Quetiapine was effective for reducing aggression in children and adolescents with ADHD when psychostimulants were inadequate. It was well tolerated with no serious side effects noted. Further randomized, controlled trials are warranted.

282E. Meta-analysis of weight effects with aripiprazole. Lyle K. Laird, Pharm.D., BCPP, Darlene Jody, M.D., Anutosh R. Saha, Ph.D., Taro Iwamoto, Ph.D., Debjit Biswas, Ph.D., Chin-Yu Lin, Ph.D., Ronald Marcus, M.D., *Robert D. McQuade, Ph.D.*; Bristol-Myers Squibb Company, Denver, CO; Bristol-Myers Squibb Company, Lawrenceville, NJ; Otsuka Maryland Research Institute, LLC, Rockville, MD; Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan; Bristol-Myers Squibb Company, Wallingford, CT.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Montreal, Canada, June 27, 2002.

283E. Safety and tolerability meta-analysis of aripiprazole in schizophrenia. *Robert D. McQuade, Ph.D.*, Elyse Stock, M.D., Stephen R. Marder, M.D., Anutosh R. Saha, Ph.D., Stephen B. Kaplita, M.S., Donald G. Archibald, M.Phil., Taro Iwamoto, Ph.D.; Bristol-Myers Squibb Company, Lawrenceville, NJ; Bristol-Myers Squibb Company, Wallingford, CT; University of California, Los Angeles, CA; Otsuka Maryland Research Institute, LLC, Rockville, MD; Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Montreal, Canada, June 27, 2002.

284E. Switching to aripiprazole monotherapy. John M. Petrias, Pharm.D., *Robert D. McQuade, Ph.D.*, Daniel E. Casey, M.D., Anutosh R. Saha, Ph.D.,

Mirza Ali, Ph.D., Darlene Jody, M.D., Mary J. Kujawa, M.D., Elyse Stock, M.D., Gary G. Ingenito, M.D.; Bristol-Myers Squibb Company, Golden Valley, MN; Bristol-Myers Squibb Company, Lawrenceville, NJ; Portland VA Medical Center, Portland, OR; Otsuka Maryland Research Institute, LLC, Rockville, MD; Bristol-Myers Squibb Company, Plainsboro, NJ; Bristol-Myers Squibb Company, Wallingford, CT.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Montreal, Canada, June 27, 2002.

285E. Aripiprazole for long-term maintenance treatment of schizophrenia. Ronald Marcus, M.D., *Neveen Abou-Gharbia, Pharm.D.*, Mary J. Kujawa, M.D., Anutosh R. Saha, Ph.D., Gary G. Ingenito, M.D., Mirza Ali, Ph.D., Xiaolong Luo, Ph.D., Donald G. Archibald, M.Phil.; Bristol-Myers Squibb Company, Wallingford, CT; Bristol-Myers Squibb Company, Lawrenceville, NJ; Bristol-Myers Squibb Company, Plainsboro, NJ; Otsuka Maryland Research Institute, LLC, Rockville, MD.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Montreal, Canada, June 27, 2002.

286E. Aripiprazole vs. placebo in the treatment of stable, chronic schizophrenia. Reenie R. Prather, Pharm.D., BCPP, Teresa A. Pigott, M.D., Anutosh R. Saha, Ph.D., Mirza Ali, Ph.D., *Robert D. McQuade, Ph.D.*, Anne F. Torbeyns, Ph.D., Elyse Stock, M.D.; Bristol-Myers Squibb Company, Steilacoom, WA; University of Florida, Gainesville, FL; Otsuka Maryland Research Institute, LLC, Rockville, MD; Bristol-Myers Squibb Company, Lawrenceville, NJ; Bristol-Myers Squibb Company, Waterloo, Belgium; Bristol-Myers Squibb Company, Wallingford, CT.

Presented at the 23rd Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Montreal, Canada, June 27, 2002.

287E. Effect of olanzapine and risperidone on glucose, lipids, and body mass. *Robert E. Litman;* Georgetown University, Rockville, MD.

Presented at the Annual Meeting of the New Clinical Drug Evaluation Unit, Boca Raton, Florida, June 10-13, 2002.

288E. Long-acting injectable risperidone: efficacy and safety. John Kane, M.D., Marielle Eerdekens, M.D., M.B.A., *Samuel Keith, M.D.*, Michael Lesem, M.D., Keith Karcher, M.S., Jean-Pierre Lindenmayer, M.D.; Hillside Hospital, Glen Oaks, NY; Janssen Research Foundation, Beerse, Belgium; University of New Mexico, Albuquerque, NM; Claghorn-Lesem Research Clinic, Bellaire TX; Janssen Research Foundation, Titusville, NJ; Manhattan Psychiatric Center, New York, NY.

Presented at the Annual Meeting of the American Psychiatric Association Institute on Psychiatric Services, Orlando, FL, October 10-14, 2001.

289E. Clozapine augmentation with risperidone in refractory schizophrenia. *Richard Josiassen, Ph.D.*, Askok Joseph, Eva Kohegyi, Wynn-Wynn Paing; Arthur P. Noyes Research Foundation, Norristown, PA.

Presented at the Annual Meeting of the New Clinical Drug Evaluation Unit, Boca Raton, Florida, June 10-13, 2002.

290E. Long-term safety and efficacy of long-acting injectable risperidone. *Marielle Eerdekens, M.D. M.B.A.*, W. Wolfgang Fleischhacker, M.D., Linda Beauclair, M.D., Stephen Martin; Janssen Research Foundation, Beerse, Belgium; Innsbruck University Clinics, Innsbruck, Austria; Clinique - Allan Memorial Institute, Montreal, Canada; Middleton St. George Hospital, Darlington County, Durham, United Kingdom.

Presented at the Annual Meeting of the American College of Neuropsychopharmacology, Waikoloa, HI, December 9-13, 2001.

291E. Olanzapine combined with mood stabilizers in prevention of recurrence in bipolar disorder: an 18-month study. Mauricio Tohen, M.D., Ph.D., Roy Chengappa, M.D., Trisha Suppes, M.D., Ph.D., Robert W. Baker, M.D., Richard C. Risser, M.S., Angela R. Evans, Ph.D., Joseph R. Calabrese, M.D., *Heidi Wirtz, Pharm.D.*; Eli Lilly & Company, Indianapolis, IN; Harvard Medical School, McLean Hospital, Belmont, MA; Western Psychiatric Institute & Clinic, University of Pittsburgh Medical Center, Pittsburgh, PA; University of Texas Southwestern Medical Center, Dallas, TX; Case Western Reserve University, Cleveland, OH.

Presented at the 40th Annual Meeting of the American College of Neuropsychopharmacology, Waikoloa, HI, December 9-13, 2001.

292E. Mirtazapine orally disintegrating tablets in depressed patients who are at least 50 years of age. *Steven P. Roose, M.D.*, Peter J. Holland, M.D., Howard A. Hassman, D.O., Murray Rosenthal, D.O.; Columbia University, New York, NY; Summit Research Network, Boca Raton, FL; Comprehensive Clinical Research, CNS, Clementon, NJ; BMR Healthquest, San Diego, CA.

Presented at the 15th Annual Meeting of the American Association for Geriatric Psychiatry; Orlando, FL, February 24-27, 2002.

Pulmonary

293. Evaluating the routine use of an asthma quality of life questionnaire in a primary care clinic. *Suzanne G. Gielow, Pharm.D.*, Candice L. Smith, Pharm.D., Theresa R. Prosser, Pharm.D.; Saint Louis College of Pharmacy, Saint Louis, MO.

PURPOSE: The National Asthma Education and Prevention Program Panel recommends monitoring of quality of life (QOL) in all asthma patients. Numerous QOL questionnaires are used in trials, but the Panel does not recommend their use due the time constraints and lack of experience in clinical practice. Our goal was to gather preliminary data about the usefulness and acceptance of the (Juniper) Mini Asthma QOL Questionnaire (15 questions) in a primary care clinic for indigent patients.
METHODS: Over 2 years, asthma patients were asked to complete the QOL survey prior to each primary care physician (PCP) visit. Exclusion criteria included: illiteracy and emergent/non-PCP visits. Total and subscale (symptoms, activities, emotion, environment) scores were calculated in a WordPerfect table.
RESULTS: Of 103 patients, 55 completed 123 questionnaires (4 illiterate, 23 no PCP visit, and 21 failed to receive the questionnaire). Two patients refused the questionnaire on 1 visit. Questionnaires were completed in approximately 5 minutes. The scores were entered and calculated in < 3 minutes. Of 27 patients completing multiple questionnaires, clinically significant improvement in total QOL score occurred in 13 (6 decreased and 8 unchanged). The average improvement (+0.74) in total QOL scores was clinically significant for this questionnaire (change ≥ 0.5).
CONCLUSIONS: Using a QOL questionnaire in a primary care clinic was accepted by patients, took minimal time and may improve QOL. This preliminary data can be used to develop more in depth studies regarding patient acceptance and clinical impact of QOL questionnaires in typical clinical practice.

Rheumatology

294. Patient satisfaction, switching, therapy modifications, and GI medication use with celecoxib compared to traditional NSAIDs in "usual" rheumatology clinical practice: the SUCCESS-IV Trial. *Eric A. Schoen, M.D.*, Michael Moriarty, M.D., Michael O'Connell, Ph.D., Dan Pettitt, DVM, M.Sc., Thomas A. Burke, Pharm.D., John G. Fort, M.D.; Kaiser Permanente Mid-Atlantic, Washington, D.C.; Waratah Corp, Durham, NC; Pfizer Inc., New York, NY; Pharmacia Corp, Peapack, NJ.

PURPOSE: To compare in OA patients randomized to celecoxib or a traditional NSAID (1) effectiveness of therapy and (2) therapy switching, therapy modifications, and GI medication use.
METHODS: In SUCCESS-IV, 450 patients with hip or knee OA requiring a change in NSAID therapy were given celecoxib or a traditional NSAID. The celecoxib arm could switch to NSAIDs, but the NSAID arm could only switch to another NSAID. Overall patient satisfaction with OA treatment and GI tolerability was assessed at the first therapy change and at 12 weeks. Responders scored a 1 (very satisfied) or 2 (satisfied) on each item (7-point scale). Moderate-to-severe pain duration, therapy switching (from baseline NSAID to another NSAID), therapy modification (therapy switch plus OA medication change), and GI medication (prescription or OTC) use were also assessed.
RESULTS: Significantly more celecoxib than NSAID patients were responders at 12 weeks (62.9% vs. 51.5%; $p<0.05$) and were "very satisfied" with OA treatment (37.1% vs. 25.8%) and GI tolerability (61.5% vs. 45.4%). Percentage of days of moderate-to-severe pain was comparable for NSAID and celecoxib users at Weeks 1-4 (43.4% vs. 39.3%), 5-8 (40.3% vs. 33.8%), and 9-12 (39.3% vs. 33.2%), respectively ($p=0.08$). Compared to NSAID users, celecoxib users had fewer therapy switches (16% vs. 22%, p=NS), therapy modifications (44% vs. 54%, $p<0.05$), therapy switches or GI medication use (50% vs. 62%, $p<0.05$), and therapy modifications or GI medication use (28% vs. 39%, $p<0.05$).
CONCLUSION: The improved satisfaction and fewer therapy switching and modifications with celecoxib may lead to improved OA treatment outcomes over time. Sponsored by Pharmacia Corporation and Pfizer Inc.

295. Retrospective evaluation of the screening and treatment of gluco-corticoid-induced osteoporosis. *Carrie L. Johnson, Pharm.D.*, Oceana Vu, Pharm.D.; Group Health Associates; University of Cincinnati, Cincinnati, OH.

PURPOSE: One study objective was to examine whether patients being prescribed long-term glucocorticoid therapy from physicians practicing in a multi-specialty group received preventive measures or were prescribed medications for osteoporosis. The second objective was to identify patient and provider characteristics associated with interventions and examine fracture rates.
METHODS: 200 patients were randomized from an original report from the group's electronic medical record showing 344 patients were on prednisone ≥

5 mg daily for at least 6 months. These charts were reviewed. However, only 132 patients were verified to be on long-term prednisone. The following interventions were recorded: otc and prescription medications for osteoporosis prevention or treatment and DEXA scans. Fracture history and other patient and provider demographics were also evaluated.
RESULTS: 54% of patients had ≥ 1 interventions aimed at osteoporosis prevention and/or treatment of osteoporosis (medications and/or DEXA scanning). Women were more likely than men to receive interventions. 35% of patients received a DEXA scan. 82% that had a DEXA had osteopenia or osteoporosis. There was a 10% fracture rate (13/132). Patients managed by rheumatologists had slightly more interventions carried out than those managed by pulmonologists or primary care physicians while rheumatologists saw just over one-fourth of the patients. 32% of patients seeing rheumatologists were being prescribed anti-resorptives. Mean age of the patients analyzed was 59.5 ± 16 years. The median prednisone length was 31 months (2.6 years).
CONCLUSION: Similar to other studies, this study shows that patients on long-term prednisone are not being adequately screening and managed for osteoporosis.

Substance Abuse/Toxicology

296E. Impact of an alcohol withdrawal practice guideline on patient outcomes in the hospital setting. Celene M. Amabile, Pharm.D., Karen M. Stanley, M.S., APRN, BC, Kit N. Simpson, Dr.PH., E. Douglas Norcross, M.D., *Cathy L. Worrall, B.S.N., R.N., Pharm.D.*; Medical University of South Carolina, Charleston, SC.

Presented at the Annual Meeting and Exposition of the American Pharmaceutical Association, Philadelphia, PA, March 15-19, 2002.

297. Sustained-release bupropion for smoking cessation in the outpatient setting. *Amy Sayner-Flusche, Pharm.D.*, Scott M. Strayer, M.D., Joshua A. Hodge, M.D.; St. Louis College of Pharmacy, St. Louis, MO; University of Virginia Health System, Charlottesville, VA; St. Louis University Belleville Family Practice, Belleville, IL.

PURPOSE: This randomized, prospective study compared smoking cessation rates of patients receiving sustained-release bupropion, as part of the Zyban Advantage Plan™ with those patients receiving bupropion in addition to intensive group behavioral modification.
METHODS: Patients who were in the "action stage" of smoking cessation (N=100) were randomized to participate either in Zyban Advantage Plan (group A) or intensive group behavioral modification (group B). Both groups received sustained-release bupropion 150 mg daily for the first 3 days followed by 150 mg twice daily for up to 3 months. Patients then followed up with their primary care physician at 1 and 4 weeks after enrollment. Telephone interviews were then conducted at 1, 3 and 6 months to determine continuous smoking abstinence.
RESULTS: At one month, 24 patients (47.1%) in group A reported they were not smoking vs. 21 (42.9%) in group B (p=0.673). Three and six month abstinence rates were 36.7% (n=18) and 25.6% (n=11) for group A compared to 31.1% (n=15) and 28.9% (n=11), respectively, for group B.
CONCLUSION: In motivated smokers receiving sustained-release bupropion, there was no difference in smoking abstinence rates between the Zyban Advantage Plan and intensive group behavioral modification.

Transplantation/Immunology

298. Comparison of valganciclovir and oral ganciclovir for cytomegalovirus prophylaxis in solid organ transplant recipients. *Alice A. Kraman, Pharm.D.*, Laura L. Hardwick, Pharm.D., Ronald S. Filo, M.D., Mahendra V. Govani, M.D., Martin L. Milgrom, M.D., Alfred J. Tector, M.D., Mark D. Pescovitz, M.D.; Clarian Health Partners; Indiana University, Indianapolis, IN.

PURPOSE: To compare efficacy, tolerability and cost of valganciclovir and oral ganciclovir when used for cytomegalovirus (CMV) prophylaxis in renal and liver transplant recipients.
METHODS: A retrospective chart review was conducted on CMV positive or negative recipients sequentially transplanted between April and November 2001 who received organs from CMV positive donors. CMV prophylaxis consisted of three months of ganciclovir 1000 mg TID or valganciclovir 900 mg QD, adjusted for renal function. Rates of CMV disease, adverse effects and cost were evaluated during the three months of prophylaxis and at least one month off prophylaxis. Adverse effects were defined as anemia (hemoglobin < 8.0 g/dl), neutropenia (absolute neutrophil count < 500/mm^3), thrombocytopenia (platelets < 50,000/mm^3), and medication discontinuation.
RESULTS: Data was collected from 61 patients (42 renal, 18 liver, and 1 liver/kidney) on valganciclovir (n=35) or ganciclovir (n=26). One patient in the ganciclovir group experiences CMV disease (p=NS). Anemia was experienced in 14% (n=5) of valganciclovir patients as compared to 23% (n=6) of ganciclovir patients (p=NS). One patient in each group had thrombocytopenia (p=NS), and one valganciclovir patient had neutropenia (p=NS). Valganciclovir was discontinued in one patient due to increased liver function tests (p=NS). For CMV prophylaxis, the average daily

299. Effects of medications that increase gastric pH on serum levels of tacrolimus in renal transplant patients. *Marie A. Chisholm, Pharm.D., FCCP,* Casandra E. Cobo, Sharita Golphin, Pharm.D., Herbert E. McGinty, B.S.Pharm., Joseph T.DiPiro, Pharm.D., FCCP; University of Georgia, Athens, GA; Medical College of Georgia, Augusta, GA.

PURPOSE: Results of in-vitro studies suggest a significant decrease in the bioavailability of tacrolimus when co-administered with medications that increase gastric pH. This study examines the influence of H_2-receptor antagonists (H_2RA), proton-pump inhibitors (PPI), sodium bicarbonate (SB), and magnesium oxide (MO) on tacrolimus serum levels in renal transplant patients.
METHODS: Patients were included in the study if they: (1) received tacrolimus-based immunosuppressive therapy for at least 1-year; (2) within that 1-year period had at least 3 months when they were not taking any H_2RA, PPI, SB, and MO, and at least 3 months when they were taking one of these medications; and (3) co-administered H_2RA, PPI, SB or MO medicines with tacrolimus. Patients' demographic data, date of transplant, weight, tacrolimus dose and serum levels, and concomitant medications were documented. Paired t-tests were used to analyze differences in average weight, daily dose (mg/kg), serum tacrolimus level, and ratio of mean daily dose (mg/kg)/mean serum tacrolimus level before and during tacrolimus use with H_2RA, PPI, SB or MO therapy.
RESULTS: The study population consisted of 12 males (66.7%), 6 females (33.3%), 11 African-Americans (61.1%) and 7 whites (38.9%). The mean age in years was 47 ± 9.6. Three patients were taking a PPI, 15 patients were taking an H_2RA, 2 patients were taking MO, and 5 patients were taking SB with tacrolimus. All patients who were taking MO and SB were on H_2RA therapy. There were no differences in mean weight (86.3 kg ± 22.97 vs. 85.4 kg ± 22.1, p=0.62), daily dose (15.3 mg ± 7.1 vs. 15.4 mg ± 7.6;p=0.93), serum tacrolimus level (11.4 ng/ml ± 3.9 vs. 10.8 ng/ml ± 3.3,p=0.56), and ratio of mean daily dose (mg/kg)/average serum tacrolimus level (0.018 ± 0.010 vs. 0.020 ± 0.013, p=0.16) before and during tacrolimus use with H_2RA, PPI, SB or MO therapy.
CONCLUSION: Patients did not experience a reduction in tacrolimus serum level when tacrolimus and H_2-receptor antagonists, proton-pump inhibitors, sodium bicarbonate, or/and magnesium oxide were co-administered.

300. Superior acute rejection prophylaxis of thymoglobulin compared to OKT3 in cadaveric and living-unrelated renal transplants. *Lonnie D. Smith, Pharm.D.*, K. Troy Somerville, Pharm.D., Aimee Sundberg, Pharm.D., Jason Crompton, Pharm.D., John M. Holman, M.D., Ph.D., Edward W. Nelson, M.D., Fuad Shihab, M.D.; University of Utah, Salt Lake City, UT.

BACKGROUND: The purpose of this study is to compare the use of thymoglobulin (THG) to anti-CD3 monoclonal antibody (OKT3) for induction therapy.
METHODS: A retrospective review of consecutive cadaveric (CAD) and living-unrelated (LURD) renal transplants from 5/30/99-5/30/01. Immunosuppression consisted of cyclosporine or tacrolimus combined with azathioprine or mycophenolate mofetil and corticosteroids. Induction was OKT3 5 mg for 10 days or THG 3 doses of 1.5 mg/kg/dose. Scr after transplant, early readmission's, infection, incidence of rejection at 3 and 6 months, and graft loss at 6 months were evaluated.
RESULTS: The OKT3 group included 38 pts (24 male, 33 CAD, 5 LURD and 5 re-transplants) the THG group included 37 pts (26 male, 34 CAD, 3 LURD, and 9 re-transplants). Four deaths occurred in the OKT3 group, none in the THG group. Three died from infectious causes one cardiac related. Two lost their grafts in the THG group one to B cell lymphoma, and one stopped his medications. Mean follow-up was 21.8 ± 5.7 months for the OKT3 group and 10.1 ± 3.4 months for the THG group. At 6 months 29% vs. 5% p=0.017 had a rejection and 5% vs. 2% lost their graft in the OKT3 and THG groups respectively. There were 6 CMV related admissions in the OKT3 group vs. 3 in the THG group.
CONCLUSIONS: THG induction resulted in a statistically significant decrease in acute rejection episodes at six months. In addition, the three-dose THG protocol resulted in a significant cost savings compared to OKT3. Longer follow-up is needed to assess the impact of THG induction on pharmacoeconomics and chronic allograft nephropathy.

301. Impact of financial issues on medication compliance after solid organ transplantation. *K. Troy Somerville, Pharm.D.*, Kim Phillips, MSN, R.N., Lonnie D. Smith, Pharm.D., Susan Pett, MSW, Fuad S. Shihab, M.D.; University of Utah Health Sciences Center, Salt Lake City, UT.

PURPOSE: The high cost of transplantation impacts all transplant recipients. The relationship between the cost of post-transplant medications and medication compliance has not been fully investigated.
METHODS: We sent a mail-survey to all transplant recipients with a

functioning allograft identified by clinic and UNOS records excluding pediatric recipients (<18 years). Responses were collected anonymously.
RESULTS: A total of 589 surveys were mailed and 292 (50%) were returned, of those, 290 (49%) could be analyzed. Respondents included kidney (72%), heart (21%), and lung (7%) recipients. At the time of the survey, 30% of respondents reported that they were currently having trouble paying for medications. A larger number (40%) reported having trouble paying for medications at some time point after transplantation. Interestingly, over 50% of patients having trouble paying for medications did have insurance coverage. Medication noncompliance due to cost issues alone was reported by 18% of respondents. The most commonly missed medications were immunosuppressants (53%), antihypertensives (46%), and lipid-lowering medications (33%). Medical complications were reported by 54% of the noncompliant patients. Complications noted on the surveys included: rising blood pressure (50%), worsening diabetes (29%), and elevated serum creatinine (24%). Regardless of noncompliance, an alarming 21% of recipients reported missing "basic necessities" to pay for medications, and 26% decided against taking a job or receiving job training for fear of losing Medicare/Medicaid funding.
CONCLUSION: The high cost of medications following solid organ transplantation definitely impacts transplant recipients. Financial issues can lead to medication noncompliance and medical complications after transplantation.

302. Pharmacokinetic study of mycophenolic acid in Korean kidney transplant patients. *Eun Kyung Cho, M.S.,* Jung M. Oh, Pharm.D., Ok S. Park, M.S., Duck J. Han, M.D., Ph.D.; Sookmyung Women's University; Asan Medical Center; Seoul, Korea.

PURPOSE: The purpose of this study was to characterize the pharmacokinetic parameters of mycophenolic acid in Korean kidney transplant patients.
METHODS: Plasma MPA concentrations of ten Korean patients administered with suboptimal dose of MMF (750 mg BID) were measured 2 weeks after the therapy by HPLC method.
RESULTS: Plasma MPA concentration-time curve showed an early sharp peak within one hour and small second peak in some patients at 4.12 hours post-dose. Mean Cmax was 8734.65 g/ml, and mean MPA AUC was calculated as 18454.25 g•hour/ml. This AUC level was lower than the reported target range and also lower than the AUC of the Caucasians who were administered with 1000 mg twice a day. The mean fraction of free MPA which is pharmacologically active was 1600.2%. Patients' age, weight, body surface area, and renal function did not influence the MPA AUC. However, difference in AUC according to sex was statistically significant (p=0.0227). MPA free fraction seemed not to be affected by serum albumin and renal function (serum creatinine or creatinine clearance). Correlation analysis for the limited strategy of MMF therapeutic drug monitoring resulted that concentrations of pre-dose, 1 hour post-dose, and 8 hour post-dose were positively related with AUC value, and their coefficient of correlation were 0.74545 (p=0.0133), 0.68485 (p=0.0289), 0.63636 (p=0.0479), respectively. It means that peak and trough concentration can be used to estimate MPA AUC.
CONCLUSIONS: It can be recommended that full dose (1000 mg BID) of MMF should be administered in Korean kidney transplantation, particularly in men, since MPA AUC of patients who received 750 mg twice a day of MMF was below the recommended targeted range. It was found that MPA free fraction is not affected by renal function when creatinine clearance is above 40 ml/min.

303. Pharmacokinetics of mycophenolate in the early period following lung and heart transplantation. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP,* Nilufar Partovi, Pharm.D., FCSHP, Leanne Kwan, Diane Decarie, B.Sc., Andrew P. Ignaszewski, M.D., Guy Fradet, M.D., Robert D. Levy, M.D.; University of British Columbia, Vancouver, BC, Canada.

PURPOSE: The purpose of this pilot study was to evaluate the pharmacokinetics of mycophenolic acid (MPA) at 3 different times in the early period following lung or heart transplantation.
METHODS: Eight patients were entered into this open-label study. Upon administration of a steady-state morning mycophenolate mofetil (MMF) dose, blood samples were collected at 0, 20, 40, 60, and 90 minutes and at 2, 4, 6, 8, 10, and 12 hours post-dose, at 3 different times in the early post-transplant period (targeted at post-transplant days 5-7, 20-40, and 60-80, respectively, and denoted as Sampling Periods 1, 2, and 3). Total MPA concentrations were measured by a validated HPLC method with ultraviolet detection and followed by ultrafiltration of pooled samples for free MPA concentrations. Pharmacokinetic parameters were calculated by traditional non-compartmental methods.
RESULTS: Patient characteristics included: 6 males and 2 females; 4 lung and 4 heart transplant recipients; mean (± SD) age of 54 ± 11 year; and weight of 75 ± 15 kg. All patients were on prednisone and cyclosporine (with the exception of one patient on tacrolimus). Sampling Periods 1, 2, and 3 occurred on post-transplant days 19 ± 17, 60 ± 36, and 112 ± 58, respectively. Mean (± SD) parameters are as follows.

Sampling Period	ALB g/L	SrCr micromol/L	Dosage mg/day	C_{max} µg/mL	DN C_{max} µg/mL
1	34 (8)	130 (46)	2375 (518)	33.8 (12.1)	10.12 (8.39)
2	35 (5)	125 (59)	2500 (535)	37.1 (14.6)	9.11 (6.39)
3	38 (5)	135 (83)	2375 (518)	34.4 (11.6)	13.38 (9.79)

(continued)

Sampling Period	T_{max} h mg/kg/day	C_{min} µg/mL	AUC* µg*h/mL	DN AUC* µg*h/mL
1	9.42 (8.51)	2.7 (3.4)	0.17 (0.49)	38.58 (46.52)
2	7.45 (4.81)	0.7 (0.5)	0.25 (0.47)	27.58 (26.45)
3	11.11 (7.92)	1.5 (1.2)	1.06 (1.71)	48.24 (38.99)

(continued)

Sampling Period	f %	free AUC µg*h/mL	
1	37.09 (47.34)	6.6 (3.5)	3.74 (6.97)
2	22.69 (18.51)	4.7 (1.9)	1.26 (1.06)
3	38.97 (26.84)	4.9 (3.1)	2.52 (3.25)

ALB=albumin; SrCr=serum creatinine; C_{max}=maximum concentration; DN=dose-normalized to 1000 mg MMF; T_{max}=time to C_{max}; AUC=area under the curve; f=free fraction; * 0.05<p<0.1 (one-way repeated measures analysis of variance and Student-Newman-Keuls posthoc test)

Interestingly, one patient had no detectable concentrations during Sampling Periods 1 and 2 whereas the patient with the highest concentrations and AUCs was the one on concomitant therapy with tacrolimus.
CONCLUSIONS: This is the first study to systematically evaluate MPA pharmacokinetics in thoracic transplant recipients at 3 different time points during the early post-transplant period. Patients demonstrated wide variability in MPA pharmacokinetics, thus emphasizing the need to individualize dosing of MMF and to further evaluate important pharmacokinetic/pharmacodynamic parameters and endpoints that impact on clinical outcomes. Further studies involving more patients and pharmacodynamic outcomes are underway to help identify optimal MMF dosing strategies.

Urology

304. Cardiovascular safety of vardenafil, a potent, highly selective PDE-5 inhibitor in patients with erectile dysfunction; an analysis of five placebo-controlled clinical trials. *Robert A. Kloner, M.D., Ph.D.,* Puneet Mohan, M.D., Ph.D., Christiane Norenberg, Kenneth Pomerantz, Ph.D., Thomas Segerson, M.D., Stephen P. Glasser, M.D.; Good Samaritan Hospital, Los Angeles, CA; Bayer Corporation Pharmaceutical Division, West Haven, CT; Bayer AG, Wuppertal, Germany; University of Minnesota, Minneapolis, MN.

PURPOSE: The cardiovascular (CV) safety profile of vardenafil was assessed in men with erectile dysfunction (ED).
METHODS: Data were pooled from 5 randomized, double-blind Phase III trials in which 2718 men with ED for >6 months received vardenafil 5, 10, or 20 mg or placebo as needed for 12 weeks. CV-related adverse events (AEs), changes in vital signs (VS) and ECG were recorded; VS were also obtained in a subgroup receiving antihypertensive medications (HTM, data recorded 11 min to 5 h post-dose).
RESULTS: In 2605 patients valid-for-safety (vardenafil-1812, placebo-793), CV risk factors included hypertension (35%), hyperlipidemia (24%), smoking (62%), diabetes (30%), and CVD (7%). Vardenafil was associated with mild reduction in BP (-4.6/-3.1 [SBP/DBP, mm Hg]) and small increase in HR (2.0 bpm). In patients receiving placebo ± HTM (n=183), no consistent changes in BP and HR were observed. In patients receiving vardenafil ± HTM (n=520), minimal additional reductions in SBP and DBP were observed, generally similar across HTM classes (ACE-I, Ca^{++} antagonist, α or β-blockers, diuretic, and ARB). Dizziness and hypertension were equally reported by 1.0% and 2% of patients receiving placebo or vardenafil. The incidence of abnormal ECG, edema, syncope, angina, hypotension, and myocardial ischemia was 0.0-<0.6%, and was not dose-related. One patient each receiving placebo had an MI, CVA, and CV surgery. One vardenafil patient experienced MI.
CONCLUSION: In this analysis of men with ED and CV comorbidities, vardenafil exhibited a favorable CV safety profile whose incidence of CV-related AEs was similar to that of placebo.

305E. Efficacy and safety of vardenafil, a selective and potent PDE-5 inhibitor in men with erectile dysfunction: the North American Pivotal Placebo-Controlled Trial. *Wayne J.G. Hellstrom, M.D.,* Marc Gittelman, M.D., Gary Karlin, M.D., Marc Thibonnier, M.D., Thomas Segerson, M.D., Harin Padma-Nathan, M.D.; Tulane University Medical Center, New Orleans, LA; South Florida Medical Research, Aventura, FL; Lawrenceville Urology, Lawrenceville, NJ; Bayer Corporation, West Haven, CT; The Male Clinic, Beverly Hills, CA.

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Women's Health

306. Double-blind, randomized, placebo-controlled, crossover study of estradiol in premenstrual asthma. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP,*

Gina Chong, Bev Beaudin, RRT, Stephen Shalansky, Pharm.D., Tony R. Bai, M.D.; University of British Columbia; St. Paul's Hospital, Vancouver, BC, Canada.

PURPOSE: In females with premenstrual asthma (PMA): 1) to characterize asthma symptoms and pulmonary function throughout two menstrual cycles, with and without exogenous estradiol administration; 2) to determine the effect of estradiol administration on asthma symptoms, pulmonary function, quality of life, and biomarkers of airway inflammation.
METHODS: Following informed consent, 12 women with documented PMA [≥20% premenstrual worsening of asthma symptoms and/or of peak expiratory flow rate (PEFR) during a one-month screening phase] were followed for two complete menstrual cycles in a double-blind, randomized, placebo-controlled, crossover fashion. Subjects received either estradiol 2 mg or placebo orally between cycle days 23 and 28 (i.e., "premenstrually"). Throughout both cycles, subjects recorded daily morning and evening PEFR readings and asthma symptoms. They reported to our clinic on Days 8 (follicular phase), 22 (luteal phase), and 28 (premenstrually) of both the estradiol and placebo cycles (denoted as visits 1-3 and 4-6, respectively) for spirometry testing and measurement of serum estradiol and biomarkers of airway inflammation. During the two premenstrual visits (Day 28), the Asthma Quality of Life Questionnaire also was administered.
RESULTS: Patient demographics (mean ± SD) upon enrollment consisted of the following: age, 38.8 ± 7.1 year; weight, 76.7 ± 11.8 kg; height, 163.2 ± 7.0 cm; forced expiratory volume in one second (FEV_1), 2.60 ± 0.69 L; % predicted FEV_1, 85.8 ± 21.6 %; FEV_1/FVC (forced vital capacity) ratio, 0.74 ± 0.11. No notable differences were observed between the estradiol and placebo cycles in daily PEFR recordings or composite asthma symptoms scores. The area-under-the-curve (AUC) for the composite asthma symptoms versus time profile was numerically, but not statistically lower (denoting less severe symptoms) during the estradiol cycle (181.5 ± 169.6 day^{-1}) compared to the placebo cycle (245.7 ± 219.6 day^{-1}). Likewise, no significant difference in AUC values for morning PEFR or evening PEFR was found between the estradiol cycle (2188 ± 228 and 2144 ± 341 L*day/min, respectively) and the placebo cycle (2140 ± 298 and 2175 ± 365 L*day/min, respectively). Despite differences ($p<0.05$) in Day 28 estradiol concentrations (998 ± 159* vs. 263 ± 154 pmol/L) for estradiol and placebo cycles, respectively, no significant differences were found in FEV_1 (2.53 ± 0.62 vs. 2.51 ± 0.67 L), serum endothelin-1 (0.68 ± 0.42 vs. 0.70 ± 0.41 pg/mL), urinary leukotriene E_4 (315 ± 129 vs. 315 ± 126 pg/mg creatinine), urinary eosinophil protein X (87 ± 136 vs. 65 ± 81 µg/mmol creatinine), or quality of life scores [all domains (170 ± 26 vs. 174 ± 27)] for the estradiol vs. placebo cycle, respectively.
CONCLUSIONS: When examined in a double-blind, randomized, placebo-controlled, crossover fashion, exogenously-administered estradiol did not have a significant effect on PMA. As in the case of premenstrual syndrome (PMS), with up to 60% of patients reporting improvement on placebo alone, the placebo effect appears to be prominent in PMA as well. Further studies are warranted to discern underlying mechanisms for the worsening of asthma in relation to menstruation.

307. Pharmacokinetics of intravenous immunoglobulin in females with the antiphospholipid antibody syndrome. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP,* Edwina Houlihan, R.N., Leanne Kwan, Joanne Li, Mary D. Stephenson, M.D., FRCSC, M.Sc.; University of British Columbia; Children's & Women's Health Center of British Columbia, Vancouver, BC, Canada.

PURPOSE: To characterize intravenous immunoglobulin (IVIG) pharmacokinetics in females with the antiphospholipid antibody syndrome (APS), who are contemplating pregnancy. To date, no pharmacokinetic data for IVIG exist for this patient population, despite its usage in obstetrics, expense, and worldwide shortage.
METHODS: Thirteen non-pregnant females with APS, based on a history of recurrent miscarriage, participated in this pilot; 7 were part of a larger open-label pharmacokinetic study and 6 were part of a larger randomized placebo-controlled clinical trial. Of these subjects, 10 received IVIG (Gamimune N 5%) and 3 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 and underwent serial blood sampling pre-infusion and at 0.5h and 1,2,3, and 4 weeks following the dose. Serum concentrations of IgG were measured by rate nephelometry and traditional non-compartmental pharmacokinetic analysis was performed.
RESULTS: Mean (± SD) age was 35 ± 5 year (IVIG group, n=10) and 32 ± 6 year (placebo, n=3), weight was 64.4 ± 16.3 kg (IVIG) and 77.6 ± 2.4 kg (placebo). Patients in the IVIG and placebo groups had a history of 6 ± 2 and 3 ± 1 spontaneous abortions, respectively. Mean (± SD) IVIG dose was 43.1 ± 12.1 g. Pharmacokinetic parameters (mean ± SD) were as follows:

	C_{max} (g/L)	C_{min} (g/L)	$AUC_{0-\tau}$ (g•h/L)
IVIG (n=10)	26.6 ± 5.0	12.1 ± 2.2	12130 ± 1477
Placebo (n=3)	10.4 ± 3.0	9.5 ± 2.9	6220 ± 1957

The roughly-estimated contribution 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)] was 5910 g•h/L. This suggests that every gram of IVIG administered yields an estimated 137 g•h/L increase in $AUC_{0-\tau}$ (determined by dividing the difference in $AUC_{0-\tau}$ values by the mean dose) or approximately 2.1 g•h/L per kg body weight.
CONCLUSIONS: In our patient population of non-pregnant females with APS, the estimated contribution of exogenously-administered IVIG (i.e., 5910 g•h/L) to the total $AUC_{0-\tau}$ was similar to that contributed by endogenous IgG (i.e., 6220 g•h/L). These pre-pregnancy data also will be useful as baseline values to track pharmacokinetic changes that may occur with IVIG throughout pregnancy.

308. Pharmacokinetics of low molecular weight heparin and unfractionated heparin in pregnancy. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP,* Edwina Houlihan, R.N., Joanne Li, Mary D. Stephenson, M.D., FRCSC, M.Sc.; University of British Columbia; Children's & Women's Health Center of British Columbia, Vancouver, BC, Canada.

PURPOSE: The purpose of this study was to determine whether differences exist in the pharmacokinetics of low molecular weight heparin (LMWH) and unfractionated heparin (UFH) before pregnancy and during the first, second, and third trimesters of pregnancy in women with the antiphospholipid antibody syndrome (APS). To date, no systematic data exist on the effect of pregnancy on LMWH or UFH pharmacokinetics in women with APS.
METHODS: Following informed consent, women with APS, who were contemplating pregnancy, were randomized to one of two treatment groups [LMWH (dalteparin) or UFH] and taught how to self-inject their heparin subcutaneously following an empiric dosing schedule. All patients received aspirin 81 mg per day concurrently. They underwent 4 serial blood sampling days (pre-pregnancy, first trimester, second trimester, and third trimester). Blood samples were collected at 0, 0.5, 1, 2, 3, 4, 6, 8, 12, and 24 hours following a steady-state dose of LMWH and at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 8, and 12 hours following a morning dose of UFH. Plasma concentrations of heparin were measured by determining anti-factor Xa activity using an amidolytic method with chromogenic substrate. Pharmacokinetic parameters were calculated by non-compartmental methods. One-way repeated measures analysis of variance (followed by Student-Newman-Keuls test, if appropriate) was used to determine statistical significance, defined as $p \leq 0.05$.
RESULTS: We report preliminary results of 13 women (n=8 on LMWH and n=5 on UFH) who have completed the study and had a successful pregnancy. Mean (± SD) age at study enrollment was 33 ± 2 year (LMWH) and 34 ± 6 year (UFH). Patients had a history of 4 ± 1 (LMWH) and 3 ± 1 (UFH) spontaneous abortions. Pharmacokinetic parameters (mean ± SD) were as follows.

Time Period	LMWH (U 24h) UFH (U q12h)	C_{max} (U/mL)	C_{min} (U/mL)	t_{max} (hour)
Pre-pregnancy	LMWH 2500	0.28 ± 0.14[a]	0.02 ± 0.02	2.5 ± 1.3
First trimester	LMWH 2500	0.20 ± 0.14[a]	0.04 ± 0.05	3.0 ± 3.6
Second trimester	LMWH 5000	0.35 ± 0.14[a]	0.05 ± 0.03	4.1 ± 1.7
Third trimester	LMWH 7500	0.47 ± 0.12[a]	0.06 ± 0.05	4.1 ± 1.4
Pre-pregnancy	UFH 5000	0.05 ± 0.04	0.01 ± 0.02	1.5 ± 0.6
First trimester	UFH 5000	0.05 ± 0.03	0.00 ± 0.00	1.2 ± 0.7
Second trimester	UFH 7500	0.12 ± 0.06	0.03 ± 0.04	2.7 ± 0.8
Third trimester	UFH 10,000	0.10 ± 0.06	0.04 ± 0.03	2.5 ± 0.7

(continued)

Time Period	$t_{1/2}$ (hour)	$AUC_{0-\tau}$ (U*hour/mL)	$Cl_{apparent}$/kg (mL/hour/kg)
Pre-pregnancy	11.7 ± 9.7	2.71 ± 0.86[a]	16.1 ± 3.9
First trimester	10.2 ± 6.7	1.76 ± 0.86[a]	30.2 ± 17.8
Second trimester	5.5 ± 2.7	3.20 ± 1.34[a]	25.0 ± 10.7
Third trimester	7.6 ± 2.5	5.15 ± 1.55[a]	19.7 ± 4.9
Pre-pregnancy	-[b]	0.30 ± 0.14	299.7 ± 144.3
First trimester	-[b]	0.20 ± 0.14	509.5 ± 290.0
Second trimester	-[b]	0.56 ± 0.33	600.3 ± 976.4
Third trimester	-[b]	0.69 ± 0.24	195.2 ± 50.6

[a]$p<0.05$ between pre-pregnancy vs. 1st trimester, pre-pregnancy vs. 3rd trimester, 1st vs. 2nd trimester, 1st vs. 3rd trimester, and 2nd vs. 3rd trimester; [b]The $t_{1/2}$ of UFH was not calculated, due to UFH's nonlinear pharmacokinetic properties.

CONCLUSIONS: In females with APS, our current empiric dosing regimen of LMWH yielded the least and greatest drug exposure (i.e., AUC, C_{max}) during the first and third trimesters of pregnancy, respectively. Due to wide variability, no significant differences were observed before and during pregnancy in UFH's pharmacokinetic parameters. These preliminary observations, if confirmed, could lead to a change in the clinical management of pregnant patients with APS.

309. Comparison of pre-pregnancy and postpartum bone mineral density in patients on low molecular weight heparin and unfractionated heparin. *Mary H.H. Ensom, Pharm.D., FASHP, FCCP,* Sue Purkiss, M.D., Edwina Houlihan, R.N., Mary D. Stephenson, M.D., FRCSC, M.Sc.; University of British Columbia; Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: The purpose of this pilot study was compare pre-pregnancy and postpartum bone mineral density (BMD) in women with the antiphospholipid antibody syndrome (APS) who were on low molecular weight heparin (LMWH) or unfractionated heparin (UFH) throughout pregnancy.
METHODS: Following informed consent, women with APS, who were contemplating pregnancy, were randomized to one of two treatment groups [LMWH (dalteparin) or UFH] and taught how to self-inject their heparin

subcutaneously following an empiric dosing schedule: LMWH 2,500 U q24h in the first, 5,000 U q24h in the second, and 7,500 U q24h in the third trimester or UFH 5,000 U q12h in the first, 7,500 U q12h in the second, and 10,000 U in the third trimester. Patients began heparin therapy (LMWH 2,500 U q24h or UFH 5,000 U q12h) pre-pregnancy, immediately after ovulation, for up to 3 menstrual cycles. If they did not conceive within the 3 cycles, the heparin was re-instituted with a positive serum pregnancy test performed 1-2 days after a missed menses. Patients continued the heparin (at same dosage as in the first trimester) for 6 weeks postpartum. All patients received aspirin 81 mg per day concurrently. All patients had BMD (Lunar DPX) measured at the lumbar spine (L2-4) and hip, prior to initiation of heparin therapy (pre-pregnancy) and at 10 weeks postpartum. Paired t-tests were used to determine statistical significance, defined as $p \leq 0.05$.
RESULTS: We report preliminary results of 15 women (n=8 on LMWH and n=7 on UFH) who have completed the study and had a successful pregnancy. Mean (± SD) age at study enrollment was 33 ± 2 year (LMWH) and 32 ± 3 year (UFH). Patients had a history of 4 ± 1 (LMWH) and 3 ± 1 (UFH) spontaneous abortions. For LMWH, pre-pregnancy and postpartum mean BMD values were 1.21 ± 0.12 g/cm^2 and 1.12 ± 0.13 g/cm^2, respectively (L2-L4; $p<0.05$) and 0.99 ± 0.13 g/cm^2 and 0.96 ± 0.13 g/cm^2, respectively (hip; $p>0.05$). For UFH, pre-pregnancy and postpartum mean BMD values were 1.32 ± 0.11 g/cm^2 and 1.22 ± 0.12 g/cm^2, respectively (L2-L4; $p<0.05$) and 1.07 ± 0.08 g/cm^2 and 1.03 ± 0.08 g/cm^2, respectively (hip; $p<0.05$).
CONCLUSIONS: Although pre-pregnancy and postpartum lumbar spine (for patients on LMWH and UFH) and hip (for patients on UFH) BMD values were statistically different, the clinical significance of these findings are questionable and requires validation in healthy pregnant women who are not on heparin therapy.

310E. Once-daily modified release ciprofloxacin vs. conventional twice-daily ciprofloxacin for treating uncomplicated urinary tract infections. Daniel C. Henry, Jr., M.D., Ernie Riffer, M.D., Daniel C. Haverstock, *Steven F. Kowalsky, Pharm.D.*, Kamal A. Hamed, M.D., Deborah A. Church, M.D.; Foothill Family Clinic, Salt Lake City, UT; Central Phoenix Medical Clinic, Phoenix, AZ; Bayer Corp., West Haven, CT.

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311. Is pre-pregnancy body mass index predictive of the need for insulin in the treatment of gestational diabetes mellitus? *Denise D. Hopkins, Pharm.D., CDE,* Donna S. West, Ph.D., Song Hee Hong, Ph.D., Nafisa K. Dajani, M.D.; University of Arkansas for Medical Sciences, Little Rock, AR.

PURPOSE: Gestational diabetes mellitus (GDM) complicates 2-5% of pregnancies. Some patients with GDM are able to maintain normoglycemia with medical nutrition therapy alone while others require insulin. This study analyzed the relationship between pre-pregnancy body mass index (BMI) and the need for insulin in GDM.
METHODS: Data were analyzed in 91 newly diagnosed GDM patients seen in the Community Women's Clinic between June 1, 2000 and May 31, 2002. Collected demographics included patient age, race, gravity, parity, and pre-pregnancy BMI. Insulin was initiated if fasting blood glucose was > 105 mg/dL. A logistic regression model was used to examine the relationship between pre-pregnancy BMI and the need for insulin.
RESULTS: Thirty-seven patients were able to maintain acceptable levels of glycemia with diet modification while fifty-four patients required insulin. The mean BMI of patients on medical nutrition therapy alone was 30 (range: 18-48). The mean BMI of patients requiring insulin was 36 (range: 20-75). Based on the p value of the logistic regression model ($p = 0.0131$), there appears to be a significant relationship between pre-pregnancy BMI and insulin requirement.
CONCLUSIONS: The results confirmed that the degree of obesity has a strong predictive value of the need for insulin in the treatment of GDM. One unexpected finding was that 15 patients with a BMI > 30 were able to control their GDM with diet alone. This underscores the importance of nutrition counseling for newly diagnosed patients. Also, an adequate trial of medical nutrition therapy should be attempted before the consideration of insulin.

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.

312. Clinical community pharmacists overcome turf barriers to advance pharmaceutical care in a health system. *Julia A. Borgmann, Pharm.D.,* Terry A. Pence, R.Ph.; Cardinal Health System, Muncie, IN.

The provision of health care can be fragmented between the inpatient and outpatient setting with multiple health care professionals contributing to patients' care. Our Health Care System is comprised of a tertiary care hospital, primary care physician practices with outpatient pharmacies, home care, and wellness. The clinical community pharmacist (CCP) is the most accessible member of the health care team and can serve as a valuable tool to facilitate this care. We utilize our CCPs to promote adverse drug reaction reporting in our physician practices, control sample medications, and provide medication assistance programs. A pediatric CCP is a breast feeding consultant who teams with the lactation consultants to serve as an information and product resource. In our disease management programs pharmacists team with dietitians and respiratory therapists to provide asthma and lipid services. CCPs partner with wellness specialists to provide cholesterol screenings. Our CCPs are members of our Diabetes Care Center, teaching classes at our outpatient locations, providing a wide array of products, and meeting individually with patients unable to attend the classes. The pharmacist which serves the outpatient HIV population also participates in our multidisciplinary HIV clinic located at the hospital. Intervention programs by the community pharmacist to monitor the use of digoxin in the elderly, metformin use, steroid inhaler compliance, and liver function testing, can help to avoid unnecessary hospitalizations. The novel integration of CCPs with other health care professionals within a health care system can enhance the continuity of care and advance of pharmaceutical care.

313. Evaluation of an acute pain initiative in a community teaching hospital. *Dianne Brundage, Pharm.D.,* Kristine J. Peterson, R.N., MSN, Juli Jordan, R.N.; Methodist Hospital/Park Nicollet Health Services, Minneapolis, MN.

PURPOSE: During the last 4 years, our institution assessed changes made in the management of acute pain.
METHODS: A baseline survey of 69 hospitalized patients provided information on the problems in acute pain management. An interdisciplinary committee decided on goals, measurements, and methods for improvement of pain management. The Quality Resources department provided measurement of goals. Physicians, nurses and pharmacists attended education programs. Administration sent out system-wide notices of congratulations when goals were met.
RESULTS: Baseline data showed: 81% of patients had a pain score > 4 (on a 0 to 10 scale), minimal documentation of a pain assessment, prolonged waiting times for pain medication, and fears and misconceptions regarding narcotic use. Meperidine use decreased in the post anesthesia care unit from 76% to 11%, while the number of patients with pain scores of ≤ 4 increased from 43% to 89% over 3 quarters. The use of meperidine in total hip and knee replacement patients went from 69% to 0%, while the number of patients with pain scores ≤ 4 increased from 44% to 75% during the same time period. Hospital-wide meperidine use declined from 47% to ≤ 14% of all injectable opioid doses, and has remained at this level for almost two years. Ninety-one percent of patients have pain documented as the 5th vital sign.
CONCLUSIONS: Improvements in acute pain management can be made through an interdisciplinary effort. Keys to success included: support of organizational leadership, participation by all disciplines, and education supported by leaders in each discipline.

314. Drug use evaluation: intravenous amiodarone. *Jodie M. Fink, Pharm.D.,* Michael A. Militello, Pharm.D., BCPS; Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Increasing expenditures of intravenous (IV) amiodarone at our institution resulted in an interventional drug use evaluation (DUE) to determine its utilization. The goal was to identify patients on IV amiodarone suitable for oral administration or IV dose reduction. Secondarily, direct cost savings associated with pharmacy interventions were assessed.
METHODS: A prospective, chart review was performed on all adult patients initiated on IV amiodarone from October to December 2001. Pharmacy interventions were made to either change IV to oral amiodarone, or to reduce the infusion rate, when appropriate.
RESULTS: Of the 173 patients analyzed, most patients were elderly men (69% men, mean age 69.5 years), on IV amiodarone for atrial fibrillation (84%). Days of IV amiodarone use totaled 560, with an average of 3.2 days (SD: ± 3.3 days) per patient. The most common doses were 1 mg/min (302 days) and 0.5 mg/min (210 days). Two patient groups were identified for further pharmacy intervention: a) patients on oral medications receiving IV amiodarone, and b) patients on higher than recommended rates of IV amiodarone administration. Such interventions have an estimated potential cost savings of $900,000/year (average wholesale price). Seventy-seven pharmacy interventions for 63 patients were documented, 42 (55%) were accepted, with a direct pharmacy cost savings of about $41,000.
CONCLUSION: Pharmacy interventions to adjust dosing of IV amiodarone have led to significant direct cost savings, and have the potential for even greater cost minimization. Through the Pharmacy & Therapeutics Committee, pharmacy will develop a program supporting cost containment of IV amiodarone.

315. A pharmacist-managed amiodarone monitoring clinic. *Reina M. Flores, Pharm.D., BCPS,* Scott D. Troyer, Pharm.D., BCPS, Donna M. Walker, Pharm.D.; James A. Haley VA Hospital, Tampa, FL.

Amiodarone has been associated with multiple toxicities, some of which can be potentially fatal. At present, this medication is a mainstay of therapy for many patients with both atrial and ventricular arrhythmias. A pharmacist-

managed Amiodarone clinic was established to monitor the safety of amiodarone drug therapy in patients who have been previously initiated on this medication by a Cardiologist. Clinical pharmacists, who are supported by a supervising Cardiologist, see patients on a consult basis per a written protocol and scope of practice. The clinical pharmacists are responsible for interviewing each patient and assessing for drug toxicity, as well as drug interactions, knowledge of medication and compliance with therapy. The clinical pharmacists provide both written and verbal education to the patients. Electrocardiograms, pulmonary function tests, chest radiographs, ophthalmology consults, and pertinent laboratory tests are also ordered and reviewed. The supervising Cardiologist is available during clinic operation for consultation and evaluation of patients as requested by the clinical pharmacist. If the effectiveness of amiodarone is in question, patients are then referred back to the Cardiology Clinic for reassessment. Clinic visits are documented thoroughly in the progress notes, and follow up is generally every 6 months. We believe that this is a novel clinic model.

316. Effect of a pharmacist/dietitian directed cardiac risk reduction clinic on lipid indices and weight reduction in a veterans population. *Hildegarde J. Berdine, Pharm.D., BCPS,* Jon J. Vlasnik, Pharm.D., BCPS, Melissa Todorich, Pharm.D. candidate; Duquesne University, Pittsburgh, PA; Butler Veterans Affairs Medical Center, Butler, PA; Pfizer, Inc, Cranberry TWP, PA.

PURPOSE: ATP III Guidelines advocate aggressive goals for targeted patients relative to TC, LDL, TG, and HDL. Therapeutic Lifestyle Changes (TLC) are recommended to reduce risk for CHD. Weight reduction is one of these modalities. This study evaluated the impact of intensive pharmacist/dietitian counseling on goal attainment for the surrogate markers of TC, LDL, TG, HDL, and weight reduction in a veteran population.
METHODS: A total of 50 patients were enrolled in the Cardiac Risk Reduction (CRR) Clinic and followed for 6 months. The primary care provider referred patients who met these criteria: failure to achieve ATP III goals on initial or chronic treatment with diet or diet and medications, patients treated with non formulary agents, targeted primary prevention patients at high risk according to Framingham assessment. Data was collected for all visits and entered into Lipid Goal Manager (Pfizer®) for analysis.
RESULTS: Goal parameters were obtained in 20% (initial) vs. 44% (current) of the study population ($p<0.05$). Triglyceride levels >400 occurred in 32% (initial) vs. 14% (current) ($p<0.05$). A BMI $\geq$ 30 was present in 48% (initial) vs. 38% (current) ($p>0.05$).
CONCLUSIONS: The ATP III Guidelines advocate TLC and aggressive goals for lipid reduction, and HDL elevation. Intensive counseling and focused care by both a pharmacist and dietitian regarding TLC or TLC and pharmacotherapy in a CRR Clinic with close follow-up of patients at risk for CHD can reduce surrogate markers. However, a longer treatment period is needed to incorporate the lifestyle changes into the daily routine of these patients.

317. Impact of stress ulcer prophylaxis algorithm. *Coursol Christian, B.Pharm., M.Sc.,* Lacerte Melanie, B.Pharm., M.Sc., Laurier Claudine, Ph.D., Poudrette Johanne, B.Pharm., M.Sc., Sanzari Sabrina, B.Pharm., M.Sc.; Royal-Victoria Hospital; University of Montreal, Montreal, PQ, Canada.

PURPOSE: At the intensive care unit of the Royal-Victoria Hospital, we noticed that the prophylaxis for stress ulcer prophylaxis is not optimal for all patients and is sometimes overused. For these reasons, we decided to implement an algorithm of stress ulcer prophylaxis to guide the medical staff on their decision. The agents chosen for the algorithm of treatment were famotidine IV, omeprazole suspension and omeprazole tablet depending on the availability of a PO or per tube route.
METHODS: Objective, evaluate the impact of a treatment algorithm for the prescription of stress ulcer prophylaxis. Design, quasi-experimental evaluative study based on pre/post intervention without concurrent comparative group. Setting, Royal-Victoria Hospital of the McGill University Health Center. Patients, 303 admissions between 16th October 2000 and 22nd December 2000 composed the pre-intervention group and 252 admissions between 29th January 2001 and 23rd March 2001 formed the post-intervention group that was exposed to the algorithm. Measurements, the proportion and number of days of inappropriate prophylaxis, prophylaxis cost per patient and the incidence of bleeding.
RESULTS: Secondary to algorithm establishment, the proportion of inappropriate prophylaxis decreased significantly (95.7% vs. 88.2%, $p=0.033$). The number of days for inappropriate prophylaxis and the cost per patient reduced significantly ($p=0,0013$ and $p=0,003$ respectively) for all the patients. Finally, the incidence of bleeding was similar for both pre and post groups.
CONCLUSION: The establishment of an algorithm of treatment for stress ulcer prophylaxis by the pharmacist allows a reduction of inappropriate prescription and in medication cost. The use of omeprazole suspension is a good cost-effective alternative to intravenous H_2-antagonists.

318. Development and implementation of an intensive insulin regimen protocol for critically ill patients in the medical intensive care unit. Joseph E. Mazur, Pharm.D., BCPS, John J. Lewin, Pharm.D., Richard Welch, R.N., MSN, Gregory Swant, R.N., BSN, David Williamson, BSP, M.S., Charlie Strange, M.D.; University of Montreal, Montreal, PQ, Canada; Medical University of South Carolina, Charleston, SC.

PURPOSE: Aggressive control of blood glucose has been shown to decrease mortality in cardiac and critically ill surgical patients. The main goal of this process improvement (PI) project and descriptive study is to evaluate the efficacy of an intensive insulin protocol in controlling blood glucoses in critically ill patients. The protocol was recently approved for use in MICU patients.
METHODS: We initiated a comprehensive program to control blood glucose levels in the MICU by development of an intensive insulin protocol. A physician order sheet was developed with the collaborative efforts of key physicians, critical care nurses, and clinical pharmacy specialists.
RESULTS: The form outlines patient inclusion/exclusion criteria, clinical practice points, and monitoring/adjustment guidelines. The salient points to this protocol entail the evaluation of infectious and systemic inflammatory response criteria of potential candidates by the M.D. or Pharm.D., and the vigilant monitoring of blood glucoses while adhering to this regimen. Goal glucose values between 80-120 mg/dL are obtained by an insulin infusion and initial hourly glucose testing.
CONCLUSIONS: This PI initiative should provide for enhanced blood glucose control which will be first piloted in a MICU. Access to the physician order sheet will be via the hospital intranet Web site. Intended future projects include: expansion of this initiative to other ICUs and a transitional study to evaluate alternatives to insulin infusions once the patients no longer meet inclusion criteria. A comprehensive educational program to medical house staff and nursing personnel will be conducted after pilot data proves the efficacy of this approach to glycemic care.

319. The University of Minnesota center for excellence in critical care. *Henry J. Mann, Pharm.D., FCCP, FCCM, FASHP,* Gregory J. Beilman, M.D., David J. Dries, M.D., Debra J. Skaar, Pharm.D., Craig R. Weinert, M.D., Peter B. Bitterman, M.D., Faculty of the Center for Excellence in Critical Care; University of Minnesota College of Pharmacy, Minneapolis, MN.

The Center for Excellence in Critical Care is a new alliance between healthcare practitioners and researchers at the University of Minnesota, Fairview-University Medical Center and critical care practitioners in the community. The Center joins participants in a comprehensive and coordinated interdisciplinary effort to provide benefits of clinical and translational research to critically ill patients. Center membership now exceeds 40 faculty and includes critical care practitioners from the Medical School departments of surgery, anesthesiology, pediatrics, medicine and physical medicine and rehabilitation; the School of Nursing, the College of Pharmacy, the School of Public Health, the Center for Bioethics and the FUMC pharmacy and ICU units as well as Regions Medical Center, VA Medical Center, and North Memorial Medical Center.
The Center has established a set of goals directed toward the improvement of outcomes in treating the critically ill and injured: 1) to improve the patient experience, survival and quality of life, 2) to increase interdisciplinary research, 3) to improve post-graduate training in critical care, and 4) to disseminate knowledge to enhance the health and well being of all critically ill patients.
To this end the Center has developed a newsletter, sponsored seed grants, developed research proposals, established weekly critical care seminars, sponsored an annual full day regional critical care program, developed a quarterly evening dinner program, and worked with other organizations to provide critical care speakers and hold forums on critical care topics in the state.

320. Drotrecogin alfa (activated): implementing institutional guidelines for use and assessing treatment outcomes in patients with severe sepsis. *Heidi Clarke, Pharm.D.,* Theodore G. Barlows, III, Pharm.D., Caridad Machado, Pharm.D., Gary Dalin, M.S., FASHP, Richard Prager, M.D.; Baptist Hospital, Miami, FL; Nova Southeastern University, Ft. Lauderdale, FL.

BACKGROUND: The advent of drotrecogin alfa (activated) (DAA) has enhanced the treatment options for patients with severe sepsis. Due to its expense and the many contraindications/warnings for use, implementation of guidelines is necessary to ensure appropriate use of this agent.
PURPOSE: To implement appropriate use guidelines for DAA, at a non-profit, community hospital, and to assess efficacy and safety. A secondary objective was to determine cost avoidance.
METHODS: A clinical pharmacist conducted a prospective review of all medical records of patients prescribed DAA. After review of the record, the pharmacist and physician determined if the patient met the appropriate use guidelines. Efficacy was determined by mortality at 28-days or at day of discharge. Adverse events were reported. Cost avoidance was determined by the acquisition cost of DAA.
RESULTS: Twenty-three patients were prescribed DAA, 10 patients met appropriate use guidelines and received the agent, whereas 13 patients did not. The mean APACHE III score of patients in the DAA group and the non-DAA group was 98 $\pm$ 46 and 67 $\pm$ 16 ($p<0.05$, t-test), respectively. Mortality was 50% (5/10) and 15% (2/13) in the DAA group and non-DAA group, respectively. No significant bleeding events were exhibited in patients receiving DAA. Pharmacist/physician collaboration resulted in 13 patients not receiving DAA and an estimated savings of $100,000.

CONCLUSION: Guidelines for use of DAA in conjunction with prospective review by a pharmacist resulted in the appropriate use of this agent with significant cost savings.

321. Incorporation of a cardiovascular risk factor awareness program in the core curriculum of a rural Mississippi high school. *T. Kristopher Harrell, Pharm.D.*, Deborah S. King, Pharm.D., Howard T. Crenshaw, Pharm.D., Marion R. Wofford, M.D., MPH, Daniel W. Jones, M.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: The purpose of this study was to incorporate a CVD educational program in the curriculum of health classes at a rural Mississippi high school. The objectives were to assess CVD risk factor awareness and to utilize pharmacy students to emphasize the importance of routine risk factor screenings.
METHODS: Initially, a questionnaire was given to assess baseline knowledge. Throughout a one-week period sixth-year pharmacy students led classroom discussions on "knowing risk factor numbers". Those students for whom parental permission was given were also screened for blood pressure, blood glucose, cholesterol, and body mass index. Students were given a one-on-one encounter with a pharmacy student who explained risk factor numbers. To evaluate the educational effectiveness, students repeated the questionnaire four weeks later. Outcome measures included awareness rates of risk factor goals.
RESULTS: A total of 80 students participated in the screenings. Of these, 67 students completed questionnaires before and after the program. At baseline, 30% of students answered blood pressure goals correctly, and at follow-up 94% answered correctly. Likewise, for blood glucose goals, at baseline 12% of students answered correctly and 76% at follow-up. For cholesterol, 10% answered correctly at baseline and 84% at follow-up. For BMI 6% answered correctly at baseline and 73% at follow-up.
CONCLUSIONS: Utilizing pharmacy students was an effective way of teaching high school students the importance of understanding CVD risk factors. The pharmacy students were also given the opportunity to be involved at the community level to promote CVD risk factor awareness and routine screenings.

322. Medication safety program for minority, refugee, and low-income older adults. *Thomas L. Lenz, Pharm.D.*, Michael S. Monaghan, Pharm.D., Janet L. Ekeler, BSN, Allison M. Jorgensen, Pharm.D., James D. Bramble, Ph.D.; Creighton University, Omaha, NE.

A program which offers a medication safety screening survey with two levels of follow-up care, as well as culturally appropriate medication education, was started in a medium size mid-western city in an attempt to identify and assist an ever-growing minority, refugee and low-income older adult population who are at risk of illness or injury due to medication noncompliance, drug interactions, poly-pharmacy or other medication related issues. The survey was completed in English, Vietnamese, Spanish, Russian, Arabic and Bosnian languages and distributed to health and social service agencies, community health and resource fairs, cultural, community, senior and recreation centers, and church and civic groups. Follow-up phone calls were conducted to those considered "at risk" by a nurse and then by a pharmacist to resolve medication related issues. Four pharmacist conducted educational videotapes on diabetes, hypertension, depression and medication safety were produced in English, Vietnamese and Spanish and distributed to the same locations as the safety screening survey. 653 total surveys from 47 sites were completed with a mean age of 76 years (71% female). Results showed 64% did not know the purpose of all their medications, 10% took over-the-counter medications unknown to their pharmacist or physician, 12% used more than 1 pharmacy, and 7% reported having medication related problems. 100 persons answering the survey reported having diabetes mellitus. Of these surveys, 25% did not check blood sugar daily, 22% reported self adjusting their medications, and 10% had blood sugar levels out of range. 256 total follow-up calls were completed.

323E. Development of a managed care pharmacy practice residency through the collaborative efforts of academia, managed care, and the pharmaceutical industry. *Teresa B. Klepser, Pharm.D.*, Mitzi M. McGinnis, Pharm.D., Stephen W. Durst, Pharm.D., Richard Dettloff, Pharm.D., Richard Cook, Pharm.D.; Ferris State University, Big Rapids, MI; Pfizer, Inc., Grand Rapids, MI; Blue Care Network of Michigan, Grand Rapids, MI.

Presented at the National Residency Preceptors Conference of the American Society of Health-System Pharmacists, San Diego, CA, August 16-18, 2002.

324. Perceptions of medication safety and therapeutic interchange by hospital patients. *Kim L. Edmonds-Rogers, Pharm.D.*, Judy L. Enders, Pharm.D.; Florida Hospital; Pfizer, Orlando, FL.

PURPOSE: Drug spending has received heightened attention as pharmaceutical utilization and novel agents have led to a rising cost in pharmaceuticals. Therapeutic interchange or 'switch therapy' is commonly employed to curb excessive drug costs. Controversies exist as to whether cost containment is compromising quality of care. The study objectives were to: assess patient knowledge and comfort level with medication safety in the hospital setting versus at home, evaluate the impact of interchange programs on patient satisfaction and potential confusion, and gain insight into patient perspectives of pharmacy discharge counseling programs.
METHODS: A patient survey was distributed to 75 patients just prior to discharge. Patient comfort level with medications at home versus in the hospital was assessed using a Likert scale (1-very unsatisfied; 5-very satisfied).
RESULTS: A significantly lower score was demonstrated for patient comfort level regarding medication safety, knowledge of drug indication, and familiarity with side effects in the hospital versus at home ($p<0.01$). Forty patients reported having a medication switched. One-third stated the reason was unknown or due to insurance coverage. An office visit resulted in 25% of these patients, while 17% self-discontinued therapy. Overall, 58.5% of responders were dissatisfied with therapeutic interchange practice. The majority of patients (83%) reported pharmacist provided education before discharge would be valuable, and 65% wanted to have a pharmacist discharge-counseling program.
CONCLUSION: Pharmacists play an integral role in monitoring medication regimens. The potential for patient confusion and dissatisfaction from switch therapies may potentially be negated through pharmacy involvement in educational discharge program.

325. Assessment of Web-based applications for ambulatory care clinical rotations. *Melissa M. Blair, Pharm.D.*, Jennifer N. Mazur, Pharm.D., Kelly R. Ragucci, Pharm.D., Joli D. Cerveny, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate pharmacy student and resident perceptions of an innovative Web site utilized during ambulatory care rotations.
METHODS: A Web site was developed to standardize the core education and evaluation experience among four ambulatory care rotation sites. Within the Web site, an on-line anonymous survey using a 5-point ordinal scale (1-5, strongly disagree-strongly agree) was designed to evaluate navigation and content, as well as to assess overall perceptions. Over a 12-month time frame, each student and resident was instructed to complete the survey at the end of their ambulatory care rotation. Survey results were compiled and analyzed.
RESULTS: Surveys were completed by 80% of residents (12/15) and 90% of students (28/31). Overall, learners found the Web site easy to navigate without distraction (median=4). Additionally, learners found the content useful (median=4). There was a discrepancy between student and resident learners regarding specific content areas. Students found the directed reading questions and self-assessment quizzes more useful than the residents (93% vs. 75% and 79% vs. 58%, respectively). In addition, students felt more comfortable evaluating preceptors on-line (89% vs. 67%). Residents believed they would use the Web site on future rotations more frequently than students (83% vs. 57%). Both students and residents appreciated the ease of accessibility and the links to other resources. The major weakness identified was inoperable links.
CONCLUSIONS: Perceptions of a Web site utilized during ambulatory care rotations were positive. The survey results reinforce the continued use of this teaching method and will enable preceptors to make appropriate adjustments for future rotations.

326. Teaching about death and dying in the pharmacy curriculum: a student-focused approach. *Ruth Ann Subach, Pharm.D., BCPS*; Western University of Health Sciences, Pomona, CA.

BACKGROUND: Death and dying has been a component of our pharmacy curriculum since it's inception. During the early years, an instructor from the physician's assistant program taught the dynamic lecture which incorporated slides and a video describing his wife's life and death. Becoming emotionally exhausting, he declined to continue the lecture, and the topic was almost dropped from the curriculum. When this was determined, the lecture was taken over by a pharmacy practice faculty and incorporated into a homeostasis block using a student-focused approach.
METHODS: Students wrote an essay about an experience they have had with death and submitted it before the lecture. Students could choose to anonymously share their essay with the class. The lecture consisted of stages of grief, and a number of personal accounts of the faculty's experiences with death and dying. Essays were incorporated into a single document and distributed to the class after the lecture.
RESULTS: A majority of students agreed to share their essay with the class. Topics submitted included death of a family member or friend, helping someone else in coping with death, dealing with a dying patient, personal and spiritual beliefs about death and dying, or dealing with mass tragedies. Students commented that participating in this assignment helped them to deal with the death of a loved one. Others commented that it helped them put another perspective on how a pharmacist can help others dealing with death. All comments from the course evaluations about this topic were positive.
CONCLUSION: Having students reflect upon their own experiences with death and dying was a positive experience for this class, and students suggested maintaining this educational format.

327. Development and implementation of a transitional orientation experience for Pharm.D. students prior to longitudinal clerkship

experiences. *John A. Dougherty, M.B.A., Pharm.D.,* Justine S. Gortney, Pharm.D., Peter Dumo, Pharm.D.; Wayne State University, Detroit, MI.

PURPOSE: To describe the development, implementation and evaluation of the orientation clerkship at the Detroit Medical Center (DMC) for Wayne State University (WSU) Pharm.D. longitudinal students.
METHODS: Pharm.D. students at WSU have the opportunity to complete all experiential clerkships for the year at same institution. This is known as a longitudinal advanced practice program (LAPP). Students who are enrolled in LAPP at the DMC complete a 6 week orientation clerkship to prepare the student for their clinical clerkships. We sought to develop an orientation that achieves the following : familiarity with drug distribution system, application of clinical skills and knowledge, and development of communication skills. Discussions and hands on experience occurred in the following areas: drug distribution (multiple components), anticoagulation, infectious disease principles, pharmacokinetics, interpersonal skills, nutrition, pain management, toxicology, documentation, and special populations. Students rated the orientation experience.
RESULTS: A 6-week, multi-site, team-taught orientation rotation was created. The rotation included all the topics we had intended. All students completed the rotation. The clerkship experience was well received. Students felt confident in pharmacokinetic dosing , pain management, and increased understanding of both distributive and clinical services. Some students felt this experience had little value in their training as future pharmacists.
CONCLUSION: A 6-week orientation clerkship that introduces distributive, clinical, and personal skills was successfully developed. Most students find this experience beneficial, however, some do not see the relevance of such a clerkship. We will re-evaluate students' assessment of their orientation rotation after the completion of clinical rotations.

328. Inhaler technique in hospitalized patients: effect of patient education by a pharmacist. *Athagran Nakham, B.Sc., Pharm.D.,* Paveena Sonthisombat, Pharm.D., BCPS; Naresuan University, Pisanuloke, Thailand.

PURPOSE: to determine if hospitalized patient could use inhaler correctly after pharmacist intervention.
METHODS: Patients using inhaler(s) admitted with exacerbation of asthma or chronic obstructive lung disease between January 7th and February 7th, 2002 at 800-bed hospital were evaluated. Patients were asked to use inhaler and 7-step technique were determined. Pharmacist intervention consisted of discussion and correct demonstration of the device. Patients were then asked to use the device again and again after the first demonstration until they could do it correctly on that day. Pharmacist asked patients to repeat all steps again although they did correctly the day before and made correction everyday until they could do it perfectly.
RESULTS: None of twenty-one patients showed all steps correctly before intervention. Exhaling slowly via mouth (step 6) and waiting 1 minutes between puffs (step 7) were ones that patients did correctly most (71.73 %) and least (23.81 %), respectively. Exhaling slowly (step 2), inhale slowly (3-5 seconds)(step 4), hold breath for 5-10 seconds (step 5), step 6, and step 7 were shown to have significant improvement ($p < 0.05$) after intervention. Some steps had to be educated twice for patients to do it correctly. Although they did all steps right the day before, they still did some steps wrong the day after. Pharmacist had to intervene patients for three consecutive days to have all patients did all steps correctly.
CONCLUSIONS: A pharmacist could improve patients' inhaler technique by intervention repeatedly and continuously.

329. An evaluation of glycemic control and the economic impact of pharmacist-administered diabetes self-management education. *Stacy M. Prutting, Pharm.D., BCPS, CDE,* Jennifer N. Mazur, Pharm.D., CDE; Medical University of South Carolina, Charleston, SC.

PURPOSE: Clinical pharmacy services have recently expanded to include extensive Diabetes Self-management Education (DSME). The following project was conducted to evaluate the effect of pharmacist-administered DSME on glycemic control and to ascertain the economic impact on improved glycemic control.
METHODS: A literature search was conducted to establish the potential health-care costs associated with improvements in glycemic control and examples of pharmacist-administered DSME. Glycemic control, measured by Hemoglobin A_{1c} (HbA_{1c}), and the number of patients achieving a goal HbA_{1c} of <7% were measured prior to and at six months after the initiation of pharmacist-administered DSME. Cost avoidance, based on comparisons from the literature, were calculated for patients with a $1% reduction in HbA_{1c}.
RESULTS: Two hundred and nine patients were referred to the clinical pharmacists for DSME. Follow-up HbA_{1c}s were available for 171 patients. After six months of pharmacist-administered DSME, a 1.7% overall reduction in HbA_{1c} was observed. Thirty-one patients were at a goal HbA_{1c} of <7% at base-line. Following six months of pharmacist-administered DSME, a 50% increase (N=61) in the number of patients with a HbA_{1c} of <7% was achieved. Additionally, 91 patients (53%) achieved a $1% reduction in HbA_{1c}. Current estimates in the literature demonstrate that a 1% reduction in HbA_{1c} resulted in average cost-avoidance of $820/year. The total number of patients who experienced a 1% or greater reduction in HbA_{1c} represents nearly $75,000 in cost avoidance.
CONCLUSION: The provision of DSME by clinical pharmacists results in improved glycemic control and reduction in health care costs.

330. Metabolic impact of targeted diabetes care coordinated by a pharmacist in an ambulatory setting. *Maria A. Summa, Pharm.D., BCPS,* H. Gwen Bartlett, Pharm.D., Mary E. Inguanti, R.Ph., MPH, FASCP; Saint Francis Hospital and Medical Center, Hartford, CT.

PURPOSE: This study documented the impact of diabetes care coordinated by a pharmacist within an inner-city medical clinic.
METHODS: Outpatients accessing care for diabetes mellitus (DM) during a four-month period were encountered. Data collected included entry labs [HgA_{1C}, fasting and random glucose, blood pressure, total cholesterol, LDL & HDL cholesterol, triglyceride]; therapeutic recommendation rendered; exit labs [HgA_{1C}, fasting and random glucose, blood pressure, total cholesterol, LDL and HDL cholesterol, triglyceride] and number of patients progressing towards disease state goals. Entry and exit labs were compared using 2002 ADA Standards of Medical Care for Patients with Diabetes Mellitus.
RESULTS: There were 112 referrals during the time period outlined. Reasons for initial encounters included self-blood glucose monitoring (SBGM) education (38%), adherence counseling (22%), suboptimal DM regimen (10%), insulin injection education (8%), oral DM medication education (2%), and patient concern about treatment (1%). The remaining encounters were for continued care. One hundred forty seven recommendations were offered, of which 68 required PCP approval (85% were accepted). Mean HgA_{1C} was reduced by 17%; mean fasting glucose was reduced by 18%; mean total cholesterol was reduced by 9%; mean LDL cholesterol was reduced by 5%; mean triglyceride level was reduced by 13%. Seventy-three percent of patients made progress towards disease state goals.
CONCLUSION: Pharmacist-provided knowledge about SBGM, medications, and treatment modifications has a positive impact on measures of metabolic control in patients with DM. The next step will be to use these performance measures to derive the potential economic benefit of improved glycemic control in our institution.

331. Impact of a community pharmacy-based intervention to detect and modify risk factors for complications of diabetes. *Sonya R. Dvorak, Pharm.D., BCPS;* South Dakota State University, Brookings, SD.

PURPOSE: To evaluate patient and physician acceptance of a community pharmacy-based intervention to identify patients' risk factors for diabetic complications and to assess the impact of pharmacists' recommendations on patient care and risk factor modification.
METHODS: Patients with diabetes who patronized a clinic-based community pharmacy were eligible to participate. A detailed assessment (blood pressure, foot exam, fasting lipid panel, fasting glucose, urine protein, medical history) was used to generate written recommendations for the patient and their physician. The extent to which patients and physicians complied with the recommendations was assessed via a follow-up patient interview. Written surveys assessed patient satisfaction and physician perceptions.
RESULTS: Twenty patients with a mean duration of diabetes of 8.5 years and an average age of 63.5 years participated. Modifiable risk factors for complications detected included; inadequate glycemic control per patient history (50%), blood pressure > 130/80 mmHg (65%), LDL cholesterol >100 mg/dl (65%), and no daily foot care (35%). Recommendations to refer patients for diabetes education, start antiplatelet therapy, improve daily foot care, obtain evaluation by a podiatrist, and increase physical activity were well accepted (>50% compliance). When recommended by the pharmacist, 29% of physicians advanced drug therapy for glycemic control and 20% advanced hypertension therapy, although no modification of lipid therapy was observed. Sixty-seven percent of responding physicians believed the recommendations were useful and 60% believed that the pharmacist had facilitated patient care.
CONCLUSIONS: A community pharmacy-based program to detect risk factors for diabetic complications is well accepted by patients and physicians and can improve diabetes care.

332. Improving diabetes care in a rural family medicine clinic. *Miranda R. Andrus, Pharm.D.,* Lisa M. Murphey, Pharm.D., Katherine C. Herndon, Pharm.D., BCPS; Auburn University, Auburn, AL; DCH Regional Medical Center, Tuscaloosa, AL; Pfizer Inc., Birmingham, AL.

PURPOSE: This project was designed to assess the current level of care of patients with diabetes and evaluate the impact of a medical record reminder system on the provision of diabetes care in a rural family medicine clinic.
METHODS: A medical record review was conducted in patients with diabetes to assess compliance with the standards of care of the American Diabetes Association (ADA). As areas for improvement in diabetes care were identified, the pharmacist completed a diabetes management form to prompt the physician to perform ADA-recommended interventions during future encounters. A follow-up review was conducted in patients with at least one clinic visit in the six months following the intervention (n = 57).
RESULTS: The mean hemoglobin A_{1c} (HbA_{1c}) was 8.4% at baseline and 7.9%

following pharmacy intervention (p=0.071). The goal HbA_{1c} was attained in 18 and 21 patients in the pre- and post-intervention periods, respectively. A modest decline in mean systolic and diastolic blood pressures was noted (154/91 mmHg vs. 152/88 mmHg), however, the number of patients achieving the ADA blood pressure goal increased from three to eight. Twenty-nine patients received lipid profile testing prior to the intervention compared with 43 patients in the post-intervention period. The mean LDL cholesterol decreased from 122 mg/dL to 98 mg/dl following pharmacy intervention (p=0.01).
CONCLUSION: Implementation of a medical record reminder system resulted in improvement in the provision of diabetes care in a rural family medicine clinic. Care may be improved further by the implementation of a pharmacy-based diabetes management program.

333. Implementation of allergic rhinitis treatment guidelines by a clinical pharmacy call center in a group model health maintenance organization. *Stephanie M. Miller, Pharm.D.,* Julie A. Porter, Pharm.D., Kent M. Nelson, Pharm.D., David M. Barbour, Pharm.D., Troy W. Stubbings, R.Ph., Nikki M. Carroll, M.S.; Kaiser Permanente, Denver, CO.

PURPOSE: Evaluate the impact of the implementation of allergic rhinitis treatment guidelines by a clinical pharmacy call center on economic and quality outcomes.
METHODS: Medical and pharmacy records of 316 allergic rhinitis patients triaged by the Clinical Pharmacy Call Center (CPCC) (case n=86) or seen in the medical office by a physician (control n=230) between March 1, 2000 and September 30, 2001 were reviewed. Allergic rhinitis medications prescribed, medication costs, related office visits, differential diagnoses, and compliance were measured. Patient satisfaction with the CPCC was evaluated.
RESULTS: The average acquisition cost of allergic rhinitis medications was $17.92 higher for cases versus controls (p=0.0017). When the average acquisition cost of nasal corticosteroids was evaluated the two groups were not significantly different (p=0.3139). Case patients were more likely to receive a new nasal corticosteroid prescription, 90.7% versus 77.8% (p=0.0090). Compliance with medications was significantly better in the control group at two and six months, 24.4% versus 2.3% and 15.2% versus 0%, respectively (p<0.0001 for both). Differential diagnosis within two weeks of triage was not significantly different between groups. The need for subsequent allergic rhinitis office visits for six months after triage was not significantly different between cases and controls. Patient satisfaction with the telephone interaction with the CPCC was positive.
CONCLUSION: Clinical pharmacists can effectively triage and treat patients with allergic rhinitis utilizing a telepharmacy model. Whether the reduction in necessary office visits offsets the higher cost of prescriptions needs to be determined.

334E. Effect of a length of therapy guarantee contract on appropriate antibiotic use: placing a pharmaceutical manufacturer at risk. *Donna M. Chiefari*; Centrus (NMHCRx), Latham, NY.

Presented at the 14th Annual Meeting of the Academy of Managed Care Pharmacy, Salt Lake City, Utah, April 3-6, 2002.

335. Is there consistency in warfarin monitoring at different ambulatory care settings within the Veterans health system? *Christine M. Miller, Pharm.D.,* Denise Waddell, Pharm.D.; North Florida/South Georgia Veterans Health System, Gainesville, FL.

PURPOSE: This study was undertaken to evaluate the management of warfarin therapy in patients at three different ambulatory care settings within VISN8 of the Veterans Health System.
METHODS: Patients were randomly selected for review according to the location of the provider that wrote the warfarin prescription. Twelve months of warfarin monitoring were evaluated starting with the most recent INR. Time to follow-up after initiation of warfarin, after change in warfarin dose, and during stable maintenance of warfarin therapy was calculated. Average Time in Therapeutic Range (TTR), total number of INRs per patient in twelve months, and number of hemorrhagic and thromboembolic events were calculated.
RESULTS: The average TTR of patients on warfarin for more than one year, with 2 or more INR values ranged from 35% to 64%. For patients followed by MD, ARNP/PA, or PHARMD the average TTR was 35%, 53%, and 64%; the average number of INRs in the previous twelve months was 8.9, 9.8, and 13.5. For patients followed at medical centers (MC), community based outpatient clinics (CBOC), and outpatient clinics the average (OPC) the number of INRs was 13, 9, 6; the average TTR was 63%, 49%, 27%, respectively.
CONCLUSION: The data suggest that (1) TTR is greatest for patients followed in the medical centers, followed by the outpatients clinics, and then the CBOCs; (2) TTR is highest for those patients monitored by a pharmacist, followed by nurse practitioner/physician assistant, and then by physicians; (3) TTR and consistency of follow-up is greatest in pharmacist managed clinics in the medical centers than in the CBOCs or OPCs that do not have pharmacist managed anticoagulation services.

336. Pharmacist-managed anticoagulation service reduces adverse events. Christy Locke, Pharm.D., *Susan L. Ravnan, Pharm.D.,* Patricia A. Carlton, Pharm.D.; St. Joseph's Medical Center; University of the Pacific, Stockton, CA.

Optimal management of anticoagulated patients reduces adverse events improving quality of life and decreasing overall health care costs. St. Joseph's Medical Center (SJMC) shared in managed care affiliations with a local Independent Physician Association and shared in financial risk for that patient population. In October 1997 SJMC financed and implemented a pharmacist managed anticoagulation clinic (AC) to provide cost effective anticoagulation management and augment the health status of their managed care patients. In December 2000, adjustments in managed care contracts forced the termination of the AC despite improved patient outcomes. We will illustrate that pharmacist managed clinics enhanced patient outcomes and reduced hospital costs as compared to routine medical care.
METHODS: 420 patients were managed in the AC. Data was analyzed 6 months prior to and after clinic closure. The clinical endpoints were number of hospitalizations for any hemorrhagic or thromboembolic event and total hospital days accrued due to an adverse event.
RESULTS: Six months prior to clinic closure, 3 hemorrhagic events occurred amounting to 8 total hospital days. Six months after clinic closure, 14 hospitalized adverse events (7 hemorrhagic and 7 thromboembolic) occurred for a total of 74 hospital days. Given an average insurance contract price of $1,500/hospital day, under pharmacist management, the patient population incurred $12,000 in hospital costs as compared to $111,000 under physician management.
CONCLUSION: A pharmacist managed AC improved patients quality of life and decreased health care costs by substantially reducing total hospital days.

337. The development of evidence-based guidelines for erythropoietin use. Jennifer A. Stoffel, Pharm.D., *Emily E. Castelli, Pharm.D.,* Susan J. Skledar, R.Ph., MPH, Susan Guttendorf, Pharm.D., Aaron L. Steffenhagen, Pharm.D., Deanne L. Hall, Pharm.D., Kristine Schonder, Pharm.D.; University of Pittsburgh Medical Center, Pittsburgh, PA.

PURPOSE: From July to November 2001, our institution realized a 10-fold increase in purchase costs for erythropoietin (EPO) over the prior year. A therapeutic review for EPO was conducted to accomplish the following objectives: 1) create evidence based practice guidelines for EPO 2) evaluate current prescribing practices to define variant prescribing and 3) identify future initiatives to optimize EPO utilization.
METHODS: A MEDLINE search was conducted to identify all clinical trials investigating the benefit of EPO. Disease states for which results demonstrated a statistically and clinically significant improvement in outcomes were included as appropriate use in the guidelines. A point prevalence study was completed between 12/17/01 and 1/08/02 to evaluate guideline compliance and identify variant practice, by clinical indication and physician service.
RESULTS: Evidence was identified supporting EPO use for anemia associated with: chronic kidney disease, myelodysplastic syndromes, myelosuppressive chemotherapy, radiation therapy, autologous blood donation, elective nonvascular noncardiac surgery, critical illness, congestive heart failure, rheumatoid arthritis, zidovudine therapy, Jehovah's Witness surgical patients and prematurity. Investigation of EPO utilization revealed an 82% (60/73) rate of compliance with the guidelines. Of the patients not meeting the guidelines, six had anemia of chronic disease and five were critically ill and did not meet the inclusion criteria of the published clinical trials. These non-evidence-based indications contributed to in excess of $200,000 of annual EPO expense
CONCLUSIONS: This analysis suggests the majority of EPO utilization is evidence based. Target areas for improved compliance include EPO discontinuation after critical illness resolution and anemia of chronic disease.

338. Evaluation of outcomes of pharmacist-administered anticoagulation monitoring. *Jennifer N. Mazur, Pharm.D.,* Elizabeth A. Blake, Pharm.D., Kelly R. Ragucci, Pharm.D., Stacy M. Prutting, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Evaluate the outcomes associated with providing an anticoagulation monitoring service.
METHODS: Patients from three ambulatory care sites who were being followed for anticoagulation monitoring from April 1, 2001 through March 31, 2002 were identified. These patients were evaluated for hospitalizations, emergency room visits, thromboembolic events, and major/minor bleeding episodes during this time frame. Data were compiled, evaluated, and compared to an established control group.
RESULTS: A total of 259 patients were followed for one year, compared to 21 patients in the control group. The total number of hospitalizations for the monitored service was 7 (3%) compared to 7 (33%) in the control group. The total number of emergency room visits in the monitored group was 4 (1.5%). There were 3 (1.2%) reported episodes of major bleeding events resulting in hospitalization, compared to 1 (4.8%) in the control group, and 13 (5%) recorded episodes of minor bleeding in the monitored group, compared to 1 (4.8%) episode in the control group. The total number of thromboembolic events in the monitored group was 4 (1.5%), compared to 7 (33%) in the

control group. An average cost avoidance per patient-year of $701.04 in the monitored group was calculated based on hospital charges. Combined hospitalization and emergency room charges resulted in a cost avoidance of $451.91 per patient-year.
CONCLUSIONS: Consistent anticoagulation monitoring provided by clinical pharmacists has been shown to be beneficial with regard to patient outcomes. This data is consistent with current literature on anticoagulation monitoring and the cost benefit that this service provides.

339. Identification of patients at risk for adverse drug events with enoxaparin and development of a physician order form to prevent future events. *Ruth J. Perkins, Pharm.D.*, Maryanne Davis, R.Ph., M.B.A.; Saratoga Care, Saratoga Springs, NY.

PURPOSE: Our purpose was twofold: 1) to perform an enoxaparin drug use evaluation (DUE) and 2) to determine which population of patients were at risk for an adverse drug event (ADE).
METHODS: The DUE was a retrospective chart review from Jan 1, 2001-Mar 15, 2001. All patients who received a 1 mg/kg dose of enoxaparin were included. Variables collected included gender, age, weight, creatinine clearance, dose, indication, concomitant medications, and ADE's.
RESULTS: 119 patients were identified as having received enoxaparin 1 mg/kg Q12H. Six of the 61 males and 10 of the 58 females had an ADE during treatment or within 12 hours of discontinuation of enoxaparin. There was no difference between the males who had an ADE and the males who didn't. But, there were statistically significant differences among the females. Those who had an ADE were older, had lower body weights, and lower creatinine clearances ($p < 0.05$ in all cases).
CONCLUSION: Based on this, a physician order form was implemented (August 2001) to identify patients with renal impairment who may not be candidates for the 1 mg/kg dose of enoxaparin. Dosing for patients with extremes of weight is also addressed. Unfractionated heparin (UFH) is recommended as an alternative due to ease of monitoring. During the last quarter of 2001 there were 12 pharmacist interventions changing the 1 mg/kg enoxaparin dose to 0.5 mg/kg or UFH due to the order form. And there was only 1 ADE with enoxaparin. We feel the new form has helped to prevent ADE's with enoxaparin.

340. A novel approach to implement a pharmacist-based anticoagulation service. *Christopher C. Lamer, Pharm.D.*; Cherokee Indian Hospital, Cherokee, NC.

PURPOSE: The purpose of the Anticoagulation Service is to enable pharmacists who are practicing in a busy outpatient pharmacy to clinically assess and manage patients who have been prescribed warfarin. It incorporates clinical services that can be performed in a timely manner within the normal outpatient pharmacy work-flow.
METHODS: Policy and procedures were developed to nationally credential pharmacists through the Indian Health Service and the local governing board, empowering them with prescriptive authority to assess warfarin therapy and adjust warfarin dosages according to protocol. Due to the busy nature of the hospital pharmacy, the establishment of a clinic was not feasible. A service was created that could be incorporated into the standard outpatient workflow. A specialized medical record form has been developed to assist the pharmacist in collecting and assessing pertinent patient data in a quick and reliable manner.
RESULTS: After 4 years of data collection, the pharmacy based anti-coagulation service has resulted in increased provider, patient, and pharmacist satisfaction. INR values have remained within goal ranges as well as or better than previous care.
CONCLUSIONS: The implementation of the anticoagulation service has been a highly successful method of increasing clinical pharmacy services within a busy outpatient pharmacy.

341. Cost containment by centralizing growth factor dispensing and stringent clinical monitoring. *Anthony County, R.Ph., M.S.*, Steven DiCrescento, R.Ph., Dalia Abdelmacksoud, B.S., Pharm.D.; New York University Medical Center, New York, NY.

PURPOSE: The decision to centralize dispensing of epoetin alpha and filgrastim, in conjunction with continued clinical monitoring, was made after repeated unsuccessful efforts to match expenditure with usage.
METHODS: Epoetin alpha and filgrastim were removed from all pharmacy satellites except for minimum par levels to facilitate dispensing of "stat" doses. Using a "target drug study list", the designated clinical pharmacist dispenses and delivers the growth factors to nursing units on a daily basis. Weekend orders are prepared on Friday evening for individual patients and left in the satellite pharmacy. All requests for missing doses are referred to the pharmacist assigned to this project. Clinical monitoring of the appropriate use of epoetin alpha includes: hemoglobin, hematocrit, weight, indication, dose, administration frequency, and use of supplemental iron. Filgrastim orders are screened for indication, dose, administration frequency, WBC, and Absolute Neutrophil Count (ANC).
RESULTS: As a result, a success rate of over 95% was achieved in challenging missing dose requests from patient care areas. An immediate impact on the budget was realized, and the Pharmacy Department achieved a savings of approximately $100,000 within the first year. This dispensing procedure for the growth factors continues to date, and the Pharmacy Department continues to realize tremendous cost savings from being able to accurately match expenditure with usage.
CONCLUSION: Epoetin alpha and filgrastim are costly items and consequently, do have a high propensity for diversion in addition to their potential for inappropriate use. This method has proved effective in drastically reducing unnecessary costs associated with procuring and dispensing growth factors.

342. Implementation of pharmaceutical care services in an HIV high-risk pregnancy clinic. *Patty Fan-Havard, Pharm.D.*, Eric J. Knudtson, M.D., Sheila K. Kang, Lakshmi Vasist, Jennifer W. Jende, Michael Para, M.D., Michael Brady; Ohio State University, Columbus, OH.

Women constitute the fastest growing population at risk for HIV infection in the United States. Combination antiretroviral therapy (ART) is now routinely recommended in pregnant HIV-1 infected women to improve maternal health and reduce HIV-1 perinatal transmission by maximally suppressing maternal viral load. Antiretroviral therapy is associated with numerous complexities including pill burden, drug-food and drug-drug interactions, and adverse events. Adherence to ART is critical to achieve optimal virologic suppression and immune preservation, prevent vertical transmission, and delay drug resistance. A multidisciplinary clinic was established in July of 2001 to improve maternal and fetal well being by providing comprehensive obstetrical , medical and pharmaceutical care to women with HIV infection. This study describes the pharmaceutical services implemented at a HIV-High Risk Pregnancy Clinic (HHRPC). All pregnant women with HIV infection, who are ART naïve, are referred to a HIV-specialist for initiation of therapy. A protocol, congruent to the Public Health Services (PHS) guidelines, has been established in collaboration with a HIV-specialist to monitor for virologic and immunologic responses and ART-related complications. Patients are interviewed by a pharmacist 15 to 20 minutes before the scheduled obstetrical visit. Pharmaceutical services provided by a pharmacist include 1) counseling about perinatal transmission risks; 2) evaluating ART efficacy; 3) evaluating and managing ART-related complications; 4) counseling on adherence to ART, 5) monitoring for drug-drug and drug-food interactions; 6) counseling on intrapartum and postpartum chemoprophylaxis, 7) modifying ART in consultation with a HIV-specialist, 8) maintaining a database on patient demographics, HIV-related laboratory values and conditions, and maternal and newborn outcomes, and 7) reporting outcomes to the National Antiretroviral Pregnancy Registry. The pharmaceutical services have been successfully implemented and the patient demographics and outcome data will be presented at the poster.

343. Development of an HIV antiretroviral order form in a tertiary care teaching hospital. *John J. Faragon, Pharm.D.*, Douglas G. Fish, M.D., Peter J. Piliero, M.D., Timothy S. Lesar, Pharm.D., Ellie Cioppa, M.S.; Albany College of Pharmacy; Albany Medical College; Albany Medical Center Hospital, Albany, NY.

PURPOSE: Published data from our institution revealed that prescribing errors related to antiretroviral therapy increased from 2% of HIV admissions in January 1996 to 12% of HIV admissions in October 1998. The most common errors were related to incorrect dosage (25.5%) and dosing frequency (30.3%). A standardized HIV antiretroviral order form was developed to simplify ordering and to reduce the frequency of prescribing errors associated highly active antiretroviral therapy (HAART).
METHODS: The study hospital is a 631-bed tertiary care teaching hospital located in upstate New York. The standardized HIV antiretroviral order form was developed by an HIV clinical pharmacy specialist and reviewed by HIV attending physicians, pharmacists, and nurses familiar with HAART prescribing. The form includes selections for standard dosage regimens for nucleoside and nucleotide reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, single and dual protease inhibitors and dosage recommendations for use in patients with end organ damage. Dietary restrictions and available dosage forms with each agent are also included.
RESULTS: Development of the HIV antiretroviral order form was completed and approved for use in June 2002. The order form is available on the hospital intranet and can be easily downloaded by students, residents, and attending physicians when prescribing HAART. An evaluation of prescribing errors associated with HAART is on-going to determine the impact of the order form on the incidence of errors.
CONCLUSIONS: In response to HAART prescribing errors, an HIV antiretroviral order form was developed to simplify HAART prescribing and reduce associated medication prescribing errors.

344. Collaborative practice for the management of hepatitis C patients in a multi-specialty medical office. *Richard H. Parrish, II, Ph.D., BCNSP*, Bernard J. Dunn, Mark Galbraith, M.D.; Shenandoah University; Selma Medical Associates, Winchester, VA.

A collaborative practice between a pharmacy practice faculty member and a community-based infectious disease specialist for the management of patients

with chronic hepatitis C is described. After physician diagnosis of hepatitis C, patients are referred for disease and treatment education. Three pre-treatment visits are conducted. Visit 1 is focused on informed consent issues, hepatitis and therapy education, social support systems, work-up of drug therapy, and insurance issues. Visit 2 is concerned with subcutaneous injection technique and practice with saline, dose calculations and prescription generation, pre-injection considerations and collection of baseline hematology and biochemistry. At visit 3, the patient prepares and administers the first dose of pegylated interferon subcutaneously. During the first month of treatment, patients are seen 3 times (at weeks 1, 3, and 4 of treatment) in the office for evaluation and management, and monthly thereafter for 5 months. At the 6 month visit, viral load is measured. Depending on genotype and viral load reduction (at least 1 log reduction), treatment continues for 6 additional months. At each visit, patients are monitored for drug therapy problems. Emergent problems are referred to the infectious disease physician for medical management. Dosage calculations and modifications for ribavirin and pegylated interferon are initiated by the clinical pharmacist using protocols from pharmaceutical labeling.

345. Implementation and evaluation of a pharmacist-managed service for the treatment of anemia of chronic kidney disease. Greg S. Bradford, Pharm.D., Carin T. Rutland, Pharm.D., Christi T. Hightower, Pharm.D. candidate, Alison C. Irwin, Pharm.D., Daniel H. Gillis, III, Pharm.D., *Shannon M. Lee, Pharm.D., BCPP,* Katherine C. Herndon, Pharm.D., BCPS; Princeton Baptist Medical Center; Samford University; Pfizer Inc., Birmingham, AL.

PURPOSE: This project is designed to 1) describe the implementation of a novel pharmacist-managed anemia service at a large community hospital, and 2) evaluate clinical and pharmacoeconomic outcomes over six months before and after implementation of this service.
METHODS: A medical record review was conducted in erythropoietin-treated patients with a primary or secondary diagnosis of chronic kidney disease who were admitted to the hospital between July 1 and December 31, 2000 (n = 165). An anemia management protocol based on current National Kidney Foundation Disease Outcomes Quality Initiative guidelines was implemented by the clinical pharmacy service in September 2001. Data collection was continued in chronic kidney disease patients who were managed by the pharmacy service from October 1, 2001 to March 31, 2002 (n = 152).
RESULTS: The pre-protocol evaluation revealed significant variation in erythropoietin and intravenous iron prescribing patterns. Mean erythropoietin doses declined following implementation of the anemia management protocol (150 units/kg pre-protocol vs. 112 units/kg post-protocol). Intravenous iron replacement therapy was prescribed in 6.7% of the pre-protocol patients and 56.6% of the post-protocol patients. A mean hemoglobin value ≥ 11 g/dL was attained in 12.1% of pre-protocol patients and 20.4% of post-protocol patients (p=0.045). Mean drug costs per patient were $722 in the pre-protocol period and $667 following protocol implementation.
CONCLUSION: Implementation of the anemia management service resulted in lower doses of erythropoietin, increased utilization of intravenous iron, and an increase in mean hemoglobin values. Additionally, mean drug costs per patient decreased following protocol implementation.

346. Use of oral ondansetron versus intravenous ondansetron as initial antiemetic therapy in oncology patients receiving moderate to highly emetogenic regimens. *William Ruspantini, M.S., R.Ph.,* Steven DiCrescento, R.Ph., Dalia Abdelmacksoud, B.S., Pharm.D.; New York University Medical Center, New York, NY.

PURPOSE: Several studies demonstrate the cost efficacy and therapeutic equivalency of oral formulations of $5HT_3$ antagonists versus the intravenous form in moderate to highly emetogenic chemotherapy regimens. The oral form provides convenient dosing, decreased administration time and supplies, and improved quality of life. The purpose of the study is to maximize the use of oral ondansetron versus the intravenous form.
METHOD: Extensive efforts were undertaken to educate the medical community and Oncology Nurse Specialists on the advantages of oral ondansetron in moderate or highly emetogenic chemotherapy. Anti-emetic guidelines were developed by the Departments of Oncology/Hematology, Medicine and Pharmacy. A list of patients receiving ondansetron was reviewed daily. The Oncology Clinical Pharmacist assessed response to oral ondansetron 24-48 hours after chemotherapy. Parameters evaluated include: emetogenic potential of chemotherapy based on the Hesketh algorithm, ondansetron dose, steroid therapy, tolerance of oral ondansetron, previous compliance and cost savings. Outcome measures include: incidence of nausea and vomiting, ability to ambulate and consume meals.
RESULTS: Twenty-seven patients were assessed prior to a chemotherapy cycle with moderate to highly emetogenic chemotherapy. Eighty-one percent of the patients were chemotherapy naïve and 19% were non-chemotherapy naïve. Eighty-five percent of the patients received highly emetogenic and 15% received moderately emetogenic chemotherapy. One patient received steroid therapy. Seventy-seven percent of the patients demonstrated complete response and 23% demonstrated major response (mild nausea occurred). All patients were able to eat and ambulate.
CONCLUSION: Oral ondansetron provides control of nausea and vomiting comparable to intravenous ondansetron with an associated substantial cost savings.

347. Multidisciplinary quality improvement initiative for cardiovascular disease and stroke in the family medicine center. *Andrea M. Wessell, Pharm.D.,* Elizabeth W. Blake, Pharm.D., Steve M. Ornstein, M.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: This project evaluated an intervention to improve adherence with clinical practice guidelines for cholesterol screening, diabetes, and hypertension in an academic Family Medicine Clinic. The project was modeled after "Practice Partner Research Network-Translating Research into Practice (PPRNet-TRIP)", an AHRQ-funded study designed to improve adherence with process and outcome measures for the prevention of cardiovascular disease and stroke in primary care practices.
METHODS: Adherence with guidelines was determined from data in the electronic medical record (EMR). Interventions were selected to include management of diabetes, hypertension, and cholesterol screening in adult patients. Identified patients were then seen in clinic by the pharmacist and the physician. Point-of-care and letter templates were used to guide care during visits and provide patient-specific results and treatment goals. Patient outreach was performed via letters and/or telephone calls. Statistical analyses were performed using paired t-test and McNemar's test as appropriate.
RESULTS: In patients with hypertension (n=64), systolic BP (SBP) decreased throughout the intervention (142 to 136 mm Hg, p=0.0424) without a change in diastolic BP. Measurement of HDL (n=510) increased during the study (29% to 35%, p=0.0001). Measurement of BP, measurement and control of HbA_{1c}, BP, and LDL in patients with diabetes (n=33), and measurement of total cholesterol did not change significantly. Response to outreach varied.
CONCLUSIONS: By applying practice guidelines, this intervention produced a reduction in SBP and an increase in HDL measurement, but did not significantly alter other parameters evaluated. Study results were limited by short duration of intervention (9 months) and small sample size.

348. Implementation of a telephone-based, tablet-splitting education program in a Veterans Affairs medical center. *Ellen M. Schellhase, Pharm.D.,* Russel E. Mathis, R.Ph.; Purdue University, West Lafayette, IN; Roudebush Veterans Affairs Medical Center, Indianapolis, IN.

PURPOSE: The purpose of this program was to implement and monitor a process to provide tablet splitting education to eligible patients in order to fulfill a Veterans Administration cost-savings initiative.
METHODS: The initial target medications were atorvastatin and simvastatin due to potential cost-savings. A computer-generated list was used to determine initial patient eligibility. Medical records were reviewed to assess qualification for enrollment. Educational encounters were conducted via telephone by a registered nurse. An algorithm designed by pharmacy guided the process. During the initial telephone call, an assessment was made to ensure patient capability of utilizing a tablet splitter, and then a 14-day trial was initiated. Medication supply, tablet splitter, and educational handouts were mailed to the patient. Patients were contacted at the end of the trial to determine if they were capable of continuing tablet splitting based on their responses to interview questions. All encounters were documented in the electronic medical record.
RESULTS: After 12 weeks, 613 patients entered into the trial phase. There were 472 patients unavailable by phone, not eligible after screening, or that declined to participate in the tablet splitting program. At this time, 483 patients successfully completed the trial phase and continued tablet splitting. Implementation of tablet splitting in these patients resulted in an estimated $75,000.00 cost savings annually.
CONCLUSION: This program is an acceptable way to provide patient education on tablet splitting. This program will continue in order to provide patient education while improving cost-effective therapy for patients at this facility.

349. Documentation of clinical pharmacy interventions for pediatric patients. *Mark R. Haase, Pharm.D., BCPS,* Michelle E. Condren, Pharm.D., Sherry A. Luedtke, Pharm.D., Allyson S. Gaylor, Pharm.D., Nicholas R. Blanchard, Pharm.D., M.Ed., James C. Griener, Pharm.D.; Texas Tech University Health Sciences Center, Amarillo, TX.

PURPOSE: Documentation and characterization of clinical interventions is now essential for the justification of clinical positions in pharmacy. This project is an ongoing study of the Pediatric Practice Team's (PPT) documentation of clinical activities using a standardized documentation system and will serve to 1) Document the clinical activities of pediatric faculty, residents, and students at TTUHSC School of Pharmacy, 2) Characterize types of interventions performed, and 3) Document the impact of our pediatric pharmacy practices.
METHODS: All interventions made from January - June 2002 by the PPT will be included. Interventions are documented in an Access™ driven database at each TTUHSC School of Pharmacy campus. Types of data collected include: date, location, diagnosis, time involved, significance, drug involved, type of intervention. Faculty members review all interventions for accuracy of

documentation and appropriate significance.
RESULTS: In the first three months of 2002, 12 clinicians accounted for a total of 1154 documented interventions. Of the interventions, residents, faculty, and students made 41%, 39%, and 20%, respectively. Forty-nine adverse drug events were prevented or detected and corrected. Drug therapy change, drug monitoring, drug information, and patient counseling were the most common activities, accounting for 75% of all interventions. Additional data, at least through June 2002 will be added to current results.
CONCLUSION: The Pediatric Practice Team at TTUHSC School of Pharmacy is able to document clinical interventions using a standardized documentation system. Further analysis may help us to identify patients who are likely to require significant intervention and document the impact of pharmacist care.

350. Translation of an asthma patient education program from English to Arabic. *Paul Munzenberger, Pharm.D.*, Joseph Moshe, M.D., Jim Moore, Vicki Tutag-Lehr, Pharm.D., May Saba, Pharm.D.; Wayne State University; Arab Community Center for Economic and Social Services; American Lung Association of Michigan; Children's Hospital of Michigan, Detroit, MI.

PURPOSE: This project provided educational materials in Arabic for use in children with asthma when the patient, parent or caregiver cannot read or speak English.
METHODS: The Peter Puffer(C) asthma materials were translated from English to Arabic by the Arab Community Center for Economic and Social Services. Two physicians with Arabic as their first language independently back translated the Arabic version into English. A focus group of 5 with Arabic as their first language reviewed a revised version for readability and understanding. A survey regarding the final Arabic version was completed by selected members of the Arabic community. Survey responders consisted of 6 adults and 6 children or their caregivers with asthma, and 6 adults without asthma.
RESULTS: Elements of Peter Puffer successfully translated include information regarding: asthma pathophysiology, triggers, pets, house dust mites, cockroaches, molds, cigarette and tobacco smoke, attack warning signs, symptoms and course of action, asthma medications in general and an action plan. The focus group concluded the documents in Arabic were easily understood and readable. They recommended no further changes. All 18 survey responders indicated the Arabic documents 1) would be of benefit to patients and caregivers, 2) helped increase their understanding of asthma, and 3) should be used within the Arab community for the prevention and treatment of asthma. Seventeen of 18 responders found the documents easy to understand.
CONCLUSION: Peter Puffer was successfully translated into Arabic and provides useable written information for patients with asthma or their caregivers.

351. Comparison of pharmacy cost reduction analysis of computer-based, single event interventions versus automated problem list interventions. Dan Moellentin, Pharm.D., Michael Warmuth, R.Ph., *Shewan Aziz, R.Ph., Ph.D.*, David Crabtree, C.Ph.T., M.S., James Raczek, M.D., Eric Hartz, M.D.; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: The Cerner® software available in Pharmacy computers at Eastern Maine Medical Center (EMMC) has the capability to alert pharmacists to potential adverse drug events (ADEs) due to inappropriate drug dosage, renal dysfunction, culture and sensitivity reports, or drug-electrolyte imbalance. Two basic types of alert firings are available, such as alerts which alarm the pharmacists during order entry and review when the abnormal laboratory values are available (synchronous) and alerts that activate when the laboratory values become abnormal during inpatient stay due to changes in patient condition or status (asynchronous). More specifically, the asynchronous alerts are programmed to fire with abnormal drug-lab values (event-driven) or when a patient with a high utilization of medications (automated list) is identified. The purpose of this study was to determine the relative pharmacy drug cost return and the relative potential cost savings generated by ADE's prevention from the two types of asynchronous alerts.
METHODS: A database of interventions by EMMC pharmacists was retrospectively reviewed to determine the relative economic return of interventions initiated by either single event prompts or automated lists. Preventative single event alerts fire when abnormal drug serum concentrations are found, renal dosing adjustments are required after initial dosing, cultures and sensitivities are confirmed, or serum electrolytes are abnormal with possible drug implication. However, automated problem lists fire on the basis of presence of multiple broad negative indicators of health, such as abnormal serum albumin, platelet levels, changes in serum creatinine, and multi-system organ involvement. Single event firing prompt the clinical pharmacist to fully review and explore patient clinical status to make appropriate recommendations on that particular issue. When automated list alert fires, the clinical pharmacist performs a complete pharmacotherapy review. The event-driven and automated list interventions were reviewed for cost saving outcomes for a period of 120 days from December 1, 2001 to March 30, 2002. The cost saving outcomes are defined as cost reduction and cost avoidance. Cost reduction is measured largely as the avoidance of drug expenses. Cost avoidance is measured as predicted total drug expense (indirect saving) and reduced hospital expenses not incurred due to intervention. Methods for calculating cost-avoidance were modifications of previously reported techniques. The personnel costs to provide the clinical pharmacy services were subtracted from the calculated cost savings.
RESULTS: Interventions resulted in either cost reduction or avoidance or both. Between December 1, 2002 and March 30, 2002, there were a total of 126 interventions resulting from event-driven rule firings. The pharmacy cost reduction associated with these interventions was $11,536 with an average of $91.50 per intervention. These same interventions resulted in a cost-avoidance of $25,658 or an average of $206 per intervention. During the same period, 420 interventions resulted from automated lists requiring a comprehensive review by a clinical pharmacist. These interventions resulted in a cost reduction of $26,375 with an average of $63.00 per intervention. The cost avoidance with the later interventions was $121,380 with an average of $289.00 per intervention.
CONCLUSION: Our data suggests that a higher medication cost reduction is associated with focused single event interventions as compared to a broad-based pharmacological review induced by automated list intervention ($91.50 versus $63.00). In contrast, the in-depth pharmacological review resulted in a higher cost avoidance ($280.00 versus $206.00). Although event alerts prompted specific actions and have a relatively higher cost-reduction return, they fail to replace pharmacotherapeutic review. Both types of asynchronous rules are useful in reducing costs of potential ADEs.

352. Economic outcomes of asthma disease management: the University of Mississippi pharmaceutical care clinic experience. *Leigh Ann Ramsey, Pharm.D.*, H. Joseph Byrd, Pharm.D., Charmaine D. Rochester, Pharm.D., James J. Pitcock, Pharm.D., Elizabeth H. Hood, Pharm.D.; University of Mississippi, Jackson, MS.

PURPOSE: To determine whether Pharmaceutical Care Clinic (PCC) management of adult asthma will lower direct patient care costs.
METHODS: Prospective cohort study. Enrollment open to referred patients followed for at least 12 months. The enrolled cohort acted as its own historical control. The outcome of interest was direct costs of care associated with Emergency Department (ED) and hospital utilization; data were recovered from University Medical Center (UMC) billing records. The study interval constituted one year prior to PCC referral compared to one year after.
RESULTS: Seventy-five consecutive patients were enrolled: mean age 36.5 years, 60% male, 75% African American. The number of ED visits fell by 66 (from 170 to 104) following PCC management, accruing a cost saving of $13,960.00; and the number of hospitalizations fell by 16 (from 34 to 18), accruing a cost saving of $85,325.00. The annualized rate of cost saving per study participant was $1,324.00. All statistical comparisons were significant.
CONCLUSION: In 1998, the Health Care Financing Administration (HCFA), through the Division of Mississippi Medicaid, approved reimbursement of pharmacists for their participation in disease management. This outcome analysis reveals that cost savings accrue to the care of asthma patients enrolled in a PCC. Study limitations include a possible underestimate of ED and hospital utilization at non-UMC facilities prior to PCC referral, and an overestimate of actual cost savings after referral due to unrecovered and unanalyzed costs associated with non-UMC care. Although analysis was limited to direct costs, quality of life (QOL) data ratify the benefit of PCC asthma management.

353. Antipsychotic cost savings: utilization of medication assistance programs in a county mental health system. *Douglas Del Paggio, Pharm.D., M.P.A.*, Richard P. Singer, M.D., Bernie Mullen; Alameda County Behavioral Health Care Services, Oakland, CA.

PURPOSE: To determine the effectiveness of antipsychotic patient assistance programs (PAPs) by analyzing the application process, eligibility criteria, acceptance percentage, approval period and ultimate cost savings for a network of community mental health safety-net providers.
METHOD: A total of 320 indigent patients receiving atypical antipsychotics (olanzapine, quetiapine, risperidone) from 12 different sites were prospectively enrolled during the period 07/01/2000-06/30/2001. Data collected included the PAP application initiation, processing and eligibility determination for each patient, as well as resulting medication supply, cost and re-application process. Finally, the percentage of patients achieving third-party eligibility was tracked.
RESULTS: Each PAP was unique in regards to overall process, eligibility requirements, medication quantity supplied, and re-application. Olanzapine (n=161): 65% application approval, 614 prescriptions, and total cost savings of $157,798. Quetiapine (n=41): 61% approval, 61 prescriptions, cost savings $13,237. Risperidone (n=118): 54% approval, 176 prescriptions, cost savings $30,096. Sixty-five percent of the patients achieved third-party eligibility at 1 year.
CONCLUSIONS: Although none of the PAPs were ideal, favorable characteristics included provider eligibility determination, bulk medication shipment and streamlining information flow through a computer interface. The olanzapine PAP had the highest approval rate and associated cost savings.

354. Impact of a pharmacy-driven antibiotic renal dosing program in a large teaching institution. *Lillian Iny, M.S., R.Ph.,* Steven DiCrescento, R.Ph., Dalia Abdelmacksoud, B.S., Pharm.D.; New York University Medical Center, New York, NY.

PURPOSE: The purpose of the program is to assess the appropriateness of antibiotic doses in patients with compromised renal function and make resultant interventions, to evaluate the effect of such a program on patient safety and to determine the cost savings associated with such dose adjustments.
METHOD: The following "focus" intravenous antibiotics are assessed: imipenem/cilastatin, meropenem, piperacillin/tazobactam, levofloxacin, and ampicillin/sulbactam. These agents were chosen for their noted renal dosing profile and potential adverse effects for non-adjusted doses. Daily data collection includes: prescribed dose, start and end date of therapy, age, gender, height, weight and serum creatinine. Creatinine clearance is calculated using the Cockcroft and Gault equation. The prescribed dose is compared to the antibiotic renal dosing guidelines established at our institution. If variances existed, a recommendation is made to the prescriber to change to the appropriate dose or frequency.
RESULTS: From January 1, 2002 to May 31, 2002, a total of 360 patients received one of the five focus antibiotics and was assessed for appropriate dose/frequency by the designated clinical pharmacist. The following is a summary of these dosing assessments: 170 patients received ampicillin/sulbactam requiring 5 interventions; 62 patients received levofloxacin requiring 3 interventions; 40 patients received piperacillin/tazobactam requiring 2 interventions; 74 patients received imipenem/cilastatin requiring no interventions; 14 patients received meropenem requiring no interventions. The interventions generally consisted of a change in frequency interval or a decrease in the prescribed dose. Cost savings was minimal.
CONCLUSION: Preliminary interventions demonstrate adverse drug reaction avoidance and enhanced patient care despite minimal cost savings in drug expenditure.

355. Our Veterans Affairs pharmacist-managed heart failure clinic: 5-year evaluation and future direction. *Kathleen C. Findley, Pharm.D., MST, BCPS,* David J. Frohnapple, Pharm.D., BCPS, BCNSP; North Florida/South Georgia Veterans Health System, Gainesville, FL.

In 1997 we established a pharmacist-managed heart failure (HF) clinic. The pharmacist-practitioner is responsible for all clinic activities and our goals are to maximize medication regimens of proven efficacy, reduce morbidity and mortality, and manage co-morbidities. Ultimately, our objectives were to prolong life, improve quality of life, and decrease the cost of HF management. After 3 years of practice we selected a random sample of patients for outcome evaluation. We evaluated number of ER (Emergency Room) visits and hospitalizations, number of patients at ACE-inhibitor goal, and relative cost of treatment for six months prior to and six months after clinic enrollment. Compared to historical controls, the HF clinic patients experienced significantly fewer HF-related ER visits and hospitalizations over a six-month period. All clinic patients achieved ACE-inhibitor goal compared to 20% of the historical controls. Number needed to treat analysis demonstrated each patient treated in clinic for six months avoided one HF-related ER visit or hospitalization. Cost avoidance was calculated for the sample clinic population and this information was included in a presentation to the VA administration. As a result, a permanent 0.5 clinical pharmacy specialist-FTEE was allocated to our HF clinic. The establishment of this position will allow us to offer service to a greater number of veterans and will allow us to begin training residents and clerkship students in the clinic. The ultimate goal of these activities is the proliferation of pharmacist-managed HF clinics throughout the VA system.

356. Personal digital assistant technology to document critical care pharmacotherapy contributions. *Timothy Bosinski, Pharm.D.,* Susan Schwartz, M.D., Lucy Campbell, M.D.; University at Buffalo; Kaleida Health, Buffalo, NY.

PURPOSE: To evaluate the application of personal digital assistant (PDA) technology to the point of care as a means of documenting the contribution of a faculty member specialized in critical care pharmacotherapy.
BACKGROUND: Clinical pharmacy services in the critical care setting has been previously reported, however the rapidly changing environment of the intensive care unit provides a challenge for the documentation of all patient-focused contributions by a critical care pharmacist (CCP).
METHODS: Clinical services provided to the medical intensive care unit were documented over a nine-month period. Services were prospectively categorized and retrospectively reviewed to ensure proper classification. A database was constructed using Pendragon Forms 3.1. A CCP attended patient care rounds daily to provide clinical services. Point of care contributions were primarily provided shortly before, during or shortly after patient care rounds. Services were documented in the PDA immediately or shortly after their provision.
RESULTS: A total of 563 contributions were captured for 205 patients during the observation period. Therapeutic consultations and drug information accounted for over 75% of services provided. Anti-infective agents, vasopressors and miscellaneous agents, ranked as the top three categories of information provided. Anti-infective agents ranked as the highest agent (21%) for which information was sought in the subcategories of dosing information, interaction information, use and indication. Regarding therapeutic recommendations, anti-infective (31%) gastrointestinal (14%), and anticoagulation agents (12%) were the top three agents. CCP consultations were addressed after patient presentation by the medical resident. 160 out of 301 therapeutic consultations were accepted immediately. Nearly all the interventions were a result of direct interaction with the medical team during patient care rounds and were secondary to active participation during patient care rounds.
CONCLUSIONS: The use of a PDA facilitates data collection and can be used to provide ongoing analysis of contributions, economic analysis and peer review for quality assurance.

357. The use of a personal digital assistant to facilitate appropriate prescribing and assessment of the use of activated protein C (drotrecogin alfa). *Linda M. Houle, Pharm.D., BCPS,* Edward Liu, M.D., Kathleen K. Casey, M.D., Michelle L. Kohute, Pharm.D.; Jersey Shore Medical Center, Neptune, NJ; Rutgers University, Piscataway, NJ.

The use of activated protein C (drotrecogin alfa) in a patient with severe sepsis requires a thorough evaluation of the patient in order to assess medication appropriateness, consider benefits and risks, and determine optimal management. In order to aid physicians in the appropriate use of activated protein C, a multidisciplinary team in our institution developed a protocol and order sheet for the prescribing of this medication. We then integrated the items on the order sheet into a handheld personal digital assistant (PDA) by creating an application in a commercially available database program (HanDBase®). We provided this program, along with applications for calculating APACHE II scores, to attending and resident physicians and clinical pharmacists involved in caring for critically ill patients. Within the database, each patient's information is organized by name and medical record number, and the data can be transferred to the PDAs of other individuals responsible for the care of the patient. Following this bedside assessment, the data is then transferred from the PDA to a desktop computer to allow for further prospective and retrospective analysis by a multidisciplinary team. Each case of severe sepsis can then be evaluated on an individual basis to determine the appropriateness of the drug and outcomes of its use on survival, length of stay in the intensive care unit, and overall length of hospital stay. By continually evaluating the use of activated protein C, the team will be able to identify potential areas for improvement with the utilization of this drug.

358. Is a doctor's visit just a doctor's visit? The role of a clinical pharmacist in a collaborative care clinic. *Tracy Baher, Pharm.D.,* Austin Bailey, M.D., Carol Pfaffly, Ph.D., Kathleen Jones, M.A., Kathy Machin, LPN, Jennifer Anderson, M.Ed.; Family Medicine Residency Program, Fort Collins, CO.

PURPOSE: Initiate an integrative, collaborative care clinic in a family medicine resident training program in order to 1) enhance resident training, and 2) meet a variety of patients' comprehensive needs.
METHODS: The team (physician, clinical pharmacist, behaviorist, wellness counselor, nurse and project coordinator) conducted three clinics over 6 weeks with faculty in preparation for resident training. The team met before and after clinic to review the patients. Patients were screened to identify needs and the team recommended specialists for each patient. The patients selected one or several team members. Patient and provider satisfaction was assessed.
RESULTS: All patients (26) were seen by the physician and nurse. Of the total, 23% (6/26), 19% (5/26), and 15% (4/26) were seen by the clinical pharmacist, wellness counselor, and behaviorist, respectively. One or more pharmacy intervention-disease/medication education, medication initiation/discontinuation, and dose increase- occurred in 23% (6/26) of the patients. A medication change occurred in 19% (5/26) of patients. A clinical pharmacy follow-up occurred for two patients. A total of 46% (12/26) responded to the patient satisfaction survey. A total of 100% of the surveyed patients and providers responded favorably to the collaborative clinic.
CONCLUSION: Collaborative clinic was proven to be an efficient and comprehensive method to see patients. This method allows patients' needs to be considered by different specialists in an interdisciplinary, collaborative manner. Patients perceived this care to be very beneficial. This is a promising method to demonstrate the multidisciplinary approach to patient care as well as teaching integrative pharmacotherapy to medical residents.

359. A model for providing cardiovascular risk assessment to community health center patients. *Laura Shane-McWhorter, Pharm.D., BCPS, FASCP, CDE, BC-ADM,* Richard H. Ensign, II, Pharm.D., BCPS, Mark A. Balk, M.D., R.Ph.; University of Utah; Pfizer, Salt Lake City, UT.

PURPOSE: Community Health Centers (CHCs) provide medical services to underserved, culturally diverse patients. The CHC patients have a high prevalence of diabetes, hypertension, and hyperlipidemia. To provide outreach education and information about cardiovascular disease to CHC patients, health fairs were conducted on a quarterly basis. At the health fairs,

patients' 10-year cardiovascular risk was calculated using a specialized software program.
METHODS: Patient demographics, health history, and the following parameters were obtained at the health fairs: blood pressure, blood glucose, and cholesterol. The information was entered into the software program, Coronary Heart Disease (CHD) Risk Factor Calculator. The program calculates 10-year risk for cardiovascular events, based on the Framingham Heart Study. Modifiable risk factors were identified and used to educate patients.
RESULTS: Cardiovascular risk assessment results were printed and given to patients, to serve as an education tool, and to convey the information to their primary care provider. Results were provided in a graph format so patients could readily understand their individualized risk. Summary reports and recommendations were given to clinic providers to increase awareness of patients' risk profiles. Recommendations included more aggressive treatment of elevated blood pressure, hyperlipidemia, and smoking cessation. Thus far, 50 patients have been evaluated and 32 (64%) are at high risk for cardiovascular disease. Patients reported an increased understanding of the various factors that may contribute to a cardiac event.
CONCLUSION: A model for providing cardiovascular information to underserved CHC patients is to use a specialized software program at health fairs. Similar services may be initiated in other patient settings.

360. The impact of anticoagulation guidelines and low molecular weight heparin therapeutic substitution on resource utilization in a community hospital. John A Noviasky, Pharm.D., Brian J Gaffney, M.D., Ather Iqbal, M.D., Jon Bushnell, R.Ph.; Mohawk Valley Heart Institute; St. Elizabeth Medical Center, Utica, NY.

PURPOSE: To describe the development and implementation of anticoagulation guidelines in a community hospital. The purpose of these actions were to positively impact the financial outcome of this facility without affecting quality of patient care.
METHODS: A low molecular weight heparin (LMWH) and unfractionated heparin (UFH) Drug Utilization Review (DUR) was completed which addressed dosing issues, Length of Stay (LOS) and bleeding comparisons. Results from this review and extensive literature search were used to develop "Anticoagulation Guidelines" in conjunction with Cardiology, Hematology, Critical Care, Family Practice and other members of the medical staff. Guidelines developed prefer Unfractionated Heparin (UFH) for all indications and use of dalteparin (rather than enoxaparin) when a LMWH is necessary.
RESULTS: The DUR (performed prior to Guideline implementation) revealed that while all UFH patients achieved therapeutic range within 24 hours using Heparin protocol, 14 patients (15%) received improper doses of enoxaparin. The Length of Stay was similar for UFH and LMWH at 6.1 ± 4.0 and 5.9 ± 4.8 (p= 0.87) days respectively and 4 UFH patients (12.5%) vs. 11 LMWH patients (16.9%) had some evidence of bleed. Six months after Guideline implementation, there was no increased LOS nor pattern change in average daily census or patient discharges for this institution. The year before implementation of Anticoagulation Guidelines, this hospital spent $550k on LMWH. Approximately one year after implementation, this institution is expending <$100k/year on this class of medication.
CONCLUSION: Implementation of Anticoagulation Guidelines has positively impacted resource utilization in this medical center without apparent effect on gross measures of outcome.

361E. Diabetes management quality improvement in a family practice residency program. *James D. Hoehns, Pharm.D., BCPS*, John E. Sutherland, M.D., Evelyn M. Hamer, R.N., Dawn M. Whitehill, Pharm.D.; Northeast Iowa Family Practice Center, Waterloo, IA; University of Iowa, Iowa City, IA.

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362. Does a language barrier impede the impact of providing pharmaceutical care in a diabetic population? *Tanya M. Konn, Pharm.D., BCPS*, Mark Drews, M.D.; Northeastern University, Boston, MA; Whittier Street Health Center, Roxbury, MA.

PURPOSE: To assess the effectiveness of providing pharmaceutical care in a community health center serving a multicultural population in which Spanish is the primary spoken language.
METHODS: After 20 months of establishing the service, a retrospective analysis of a physician referral, pharmacist-managed diabetes clinic was conducted. Eligible patients were those whom $HgbA_{1C}$ values were available 6 months prior to and 6 months after pharmaceutical intervention. Patients served as their own controls. Data on lipid levels, aspirin usage, vaccination rates and pharmacist-initiated medication changes was also collected.
RESULTS: Sixty-five patients (mean age 55.6 ± 11 years) were screened. Demographics - ethnicity: 39% African-American, 37% Hispanic, 20% unknown ethnicity, 5% other Non-Caucasian. 31% of patients were Spanish-speaking. Compared to pharmaceutical intervention, rates of aspirin usage were 32% vs. 68%. Compared prior to intervention, mean $HgbA_{1c}$ values were 9.2 ± 2.1% vs. 8.1 ± 1.7% (p=0.0001). When comparing ethnic groups, mean decrease in $HgbA_{1c}$ was 1.6 ± 1.6% Spanish-speaking, 1.2 ± 1.7% unknown ethnicity, 0.9 ± 1.7% African-American, 0.8 ± 1.2% other Non-Caucasian. Mean improvement in $HgbA_{1c}$ was similar amongst African-Americans and Spanish-speaking patients (p=0.84). Mean total cholesterol and low density lipoprotein levels (n=35) pre- and post- were 222 ± 48 mg/dL vs. 190 ± 33 mg/dL (p=0.0001) and 146 ± 42 vs. 118 ± 40 mg/dl (p=0.003) respectively.
CONCLUSION: Based on this small analysis with a limited sample size, providing pharmaceutical care to Spanish-speaking patients does not appear to be a barrier from impacting the control of diabetes.

363. Collaborating to provide free medications to underserved patients. *Melissa A. Somma, Pharm.D.*, Patricia M. Klatt, Pharm.D., BCPS, Mary Jo Auth, L.S.W., Janet St. Denis, R.Ph., Ronald O'Neill, Pharm.D.; University of Pittsburgh, Pittsburgh, PA.

PURPOSE: This pilot program aimed to 1) efficiently provide low-cost, vital medications to underserved patients in our three community health centers and 2) provide family practice residents rational choices in the sample cabinet for treating hypertension and infectious diseases.
METHODS: A multi-disciplinary team (social worker, resident and attending physicians, pharmacists, and nurses) collaborated with the outpatient pharmacy at our hospital, geographically separate from the health centers, to design a system to provide eligible patients with free medications. Medications included in the pilot were atenolol, hydrochlorothiazide, amoxicillin, cephalexin, doxycycline, erythromycin, and trimethoprim/sulfamethoxazole. Prescribing physicians complete a faxable prescription for the outpatient pharmacy. The physician provides the patient with a hand labeled "starter pack" of medication containing a 48 hour supply, and patient education handouts. The remaining supply is sent to the health center the following day for patient pick-up.
RESULTS: From February through April of 2002, a total of 99 prescriptions were filled, 97 of which were subsequently picked up at the health centers, a 97% compliance rate. The total cost for the medications including pharmacist time and dispensing materials amounted to $445.50. Both resident and attending physicians have found the program helpful in prompting more appropriate medication choices.
CONCLUSIONS: We were able to efficiently provide low-cost, vital medications to our underserved patients. With this baseline data, we secured permanent funding to sustain the program and add additional medications including albuterol inhalers and antidiabetic agents. We hope to further expand the program and measure clinical outcomes.

364. Integration of an academic pharmacy initiative and pharmacy professional experience program with a progressive community pharmacy clinical practice program. *Angela M. Wisniewski, Pharm.D.*, Cori A. Miklejn, R.Ph., Pamela A. Eppolito, R.Ph., Gene D. Morse, Pharm.D., Michael Rossi, R.Ph.; SUNY, University at Buffalo; Eckerd PatientCARE™ Centers, Buffalo, NY.

PURPOSE: To implement clinical activities within the framework of traditional community pharmacy with the goal of transitioning from dispensing-focused towards pharmaceutical care based practice by integrating a university-based clinical practice and Pharmacy Professional Experience Program.
METHODS: The University at Buffalo and Eckerd established a joint faculty position. The faculty member, two PatientCARE™, and 9 dispensing pharmacists participated. A clinically oriented clerkship experience integrated into pharmacy activities and contributed to data collection.
Clinical programs included 1) criteria-based, medication profile reviews to identify patients receiving ≥ 1 narrow therapeutic index target medication, 2) implementation of the Eckerd PatientCARE program, including two PatientCARE pharmacists, 3) fourth professional year pharmacy clerkship experiences with objective assignments, and 4) community-based health screening events in multi-resident housing complexes.
RESULTS: 1) Overall, 375 occurrences of ≥ 1 of six target medications were found, 196 profiles contained at least one potentially interacting medication. 2) At one location, 72 patients, aged 63 (± 20.5) with 3.8 (± 2.4) medical conditions were seen by PatientCARE pharmacists. 3) In total, 27 students on 39 rotations completed 1450 objective, clinical, patient-orientated assignments. 4) Of 44 individuals screened at one community event, follow-up was required for 52% (22/42) with blood pressures >139 or >89 mm Hg and 22% (8/37) with HDL <40 mg/dl.
CONCLUSIONS: Successful implementation of innovative clinical pharmacy activities in traditional community pharmacy was accomplished through the efforts of dispensing and clinical pharmacists, Doctor of Pharmacy students, the University at Buffalo, and Eckerd. Program expansion, with documentation of clinical and economic outcomes, is being utilized in the paradigm shift in community pharmacy practice.

365. Venous thromboembolism prophylaxis conversion program for hospitalized medical patients: a five-month report. *Douglas N. Carroll, Pharm.D.*; University of Oklahoma; Hillcrest Medical Center, Tulsa, OK.

PURPOSE: Recent guidelines from the American College of Chest Physicians recommend that medical patients at risk for venous thromboembolism (VTE) should receive either low-dose unfractionated heparin (LDUH) or low-

molecular-weight heparin for VTE prophylaxis. This report documents the success of a program implemented to convert medical patients from enoxaparin to LDUH for VTE prophylaxis.
METHODS: Hospitalized patients receiving enoxaparin for VTE prophylaxis during the period of November 2001 thru March 2002 were reviewed for potential conversion to LDUH. Patients excluded from conversion were those in the post-operative period, patients with a history of heparin-induced thrombocytopenia, or with evidence of minor bleeding. Data was collected for intervention acceptance rate, days of enoxaparin avoided, and the occurrence of documented VTE or significant bleeding.
RESULTS: Throughout this five-month period, 258 patients were reviewed for potential conversion to LDUH. Of these, 58 were considered to be candidates for conversion. Ten patients were discharged prior to any intervention. Of the remaining 48 patients, 37 (77%) were successfully converted resulting in an avoidance of 150 days of enoxaparin prophylaxis and an associated medication cost savings of $3123. The remaining 11 (23%) patients utilized 76 days of enoxaparin at a medication cost of $1714. No patients in the LDUH conversion group or the enoxaparin group experienced a documented VTE or significant bleed during their admission.
CONCLUSION: Patients that meet criteria can be converted from enoxaparin to LDUH for VTE prevention. This economically attractive conversion can significantly reduce drug expenditure for hospital pharmacies while following national guidelines.

366. Performing statewide medication usage evaluations utilizing handheld technology. *Dean M. Najarian, Pharm.D., BCPP*; Tewksbury State Hospital, Tewksbury, MA.

PURPOSE: To utilize handheld technology in order to provide standardized medication usage evaluation (MUE) data collection in a closed state-wide health system with consistent data collection and benchmarking capabilities between State facilities. This information is utilized to improve patient outcomes and assess disease state management in a time efficient manner.
METHODS: The clinical pharmacy team of twelve clinical specialists develops a medication usage evaluation calendar that is presented once a year to the State Pharmacy and Therapeutics (P&T) Advisory Board. The data assessment tool is developed for individual medications, groups of medications, or specific disease states that reflect current consensus guidelines or prescribing information. This tool is converted and programmed for handheld use that is accessible to each clinical pharmacist through a handheld device.
RESULTS: The handheld program converts the collected data into an easy to manage spreadsheet. The clinical team will present individual site findings and recommendations to their respective P&T Committee for discussion. The clinical director compiles a summary document, which is presented to the State P&T Advisory Board for discussion, recommendations and follow-up.
CONCLUSIONS: The use of handheld technology provides a consistent data collection tool when utilized by multiple users when compared to the traditional handwritten paper tool. Standardized reports contain important benchmarking data such as proper diagnosis, proper monitoring parameters, adverse drug reaction detection, and patient education assessment as well as documented clinical interventions to improve patient outcomes. Time efficient data collection also allows the clinical pharmacist to be available for other clinical activities.

367. The effects of pharmaceutical care on quality of care and cost on patients in a family practice residency program. Ila Mehra Harris, Pharm.D., BCPS, *Sarah Biebighauser, Pharm.D.*, James Van Vooren, M.D.; University of Minnesota, Minneapolis, MN.

PURPOSE: The primary purpose of this study was to evaluate the effect of pharmaceutical care on quality of care and cost on patients in a family practice clinic/residency program.
METHODS: Data was collected over one year on patients enrolled in a Minnesota nonprofit Health Maintenance Organization (HMO). Charts of selected patients were reviewed by the pharmacist, and patients were then seen by the pharmacist for pharmaceutical care. Each visit was fully documented into a computer software program.
RESULTS: Ninety-two patients were included in this study, with a total of 203 patient encounters. Drug therapy problems were identified in 90% of patients, for a total of 250 drug therapy problems found. Status improved in 45% of patients, 46% stayed the same, and 9% declined ($p< 0.001$). A statistically significant improvement in status from baseline to end was found in hypertension ($p=0.007$), dyslipidemia ($p=0.002$), and asthma ($p=0.011$). A higher percentage of patients reached their therapeutic goals from baseline to end for hypertension (38% vs. 62%) and dyslipidemia (21% vs. 50%), however these did not reach statistical significance. From baseline to end, significant improvement was seen for aspirin use in diabetes (57% vs. 81%, $p=0.063$), aspirin for MI prevention (50% vs. 93%, $p=0.031$), and inhaled steroids for asthma (36% vs. 64%, $p=0.031$). Polypharmacy was reduced from an average of 3.92 medications to 3.04 ($p<0.001$). The estimated total cost savings was $4,011.00.
CONCLUSIONS: Pharmaceutical care has a significantly positive impact on quality of care and cost on patients in this family practice clinic/residency program.

368. Measuring patient satisfaction with care in a neurology clinic: physician and pharmacist. Morli G. Majmudar, Pharm.D., Donna M. Givone, Pharm.D., Kiranpal S. Sangha, Pharm.D., Padmini Sekar, M.S.; University of Cincinnati, Cincinnati, OH; University of Illinois at Chicago, Chicago, IL; University of Alabama at Birmingham, Birmingham, AL.

PURPOSE: To use a patient satisfaction survey to measure patient's perception of care provided by physicians and pharmacists in a neurology clinic.
METHODS: An 11-item questionnaire was developed to measure patient satisfaction. The questionnaire contained 10 closed-ended questions and one open-ended question. Patients, following their visit with either the physician or the pharmacist at The University Hospital Neurology Clinic, filled out the questionnaire. Surveys were collected from January 2001 to July 2001 and September 2001 to April 2002. A five-point Likert scale ranging from 5 (strongly agree) to 1 (strongly disagree) was used to grade the responses.
RESULTS: A total of 201 surveys were completed (N=110 physician group, N=91 pharmacist group). Three of the ten closed-ended questions showed statistically significant results for the pharmacist group when compared to the physician group. These three questions referred to the time spent by the practitioner with the patient (4.60 vs. 4.36; $p=0.017$); the choice of words used by the practitioner (4.37 vs. 3.94; $p=0.011$); and the overall satisfaction with the visit (4.57 vs. 4.29; $p=0.023$). Additionally, the composite total score of all the ten closed-ended questions was also significant for the pharmacist group (42.08 vs. 40.03; $p=0.027$). No statistical significance was found, when data between the two groups were analyzed based on age and gender. Patients frequently commented about the long wait in the open-ended question.
CONCLUSION: The mean scores were consistently high in the pharmacist group, indicating patient satisfaction with the services provided. Patients were satisfied with the amount of time spent with the pharmacist's, and the ability of the pharmacist's to use words they could understand. This survey instrument should be used with caution until it is validated.

369. Cost analysis of a pharmacist-administered adult immunization service. *James J. Sterrett, Pharm.D.*, Melissa M. Blair, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To conduct a cost-analysis of a pharmacist administered adult influenza immunization program in a pharmacy within a family medicine clinic.
METHODS: After administering over 300 immunizations, the product and personnel costs of delivering the immunization service and the reimbursement from patients and 3rd parties were analyzed. Product costs included: medication, needles, syringes, and other supplies. Personnel costs included: appointment scheduling, shot provision and education, documentation, and billing. Personnel costs were calculated based on average time and type of personnel providing the service.
RESULTS: Average time spent providing services was as follows: 2 minutes to schedule an appointment, 5 minutes to prepare and provide the immunization, 5 minutes to document the encounter, and 5 minutes to bill, if required. Pharmacists performed all these services except for appointment scheduling which was shared with a technician. Based on an average yearly pharmacist's salary of $70,000 and technician's salary of $21,000, the per patient personnel cost of providing these services was $9.11. The product cost per patient was calculated to be $4.69. Reimbursements ranged from $8.86-$15.00 per immunization. The total cost to provide immunizations was $4208.44 and reimbursement was $3214.18. Therefore, the pharmacy lost $994.26, or $3.26 per immunization.
CONCLUSIONS: Based on the average product and personnel cost, a pharmacist administered adult influenza immunization service is not financially profitable at this pharmacy. Other benefits such as introduction of new business into the pharmacy, improving work flow to incorporate further disease state management, and changes in patient perception of pharmacists were not measured.

370. Patient cost savings through the use of pharmaceutical manufacturer assistance programs in a private ambulatory care setting. *Mahnaz Sarrafizadeh, Pharm.D.*, Nancy M. Waite, Pharm.D., Eric H. Hobson, Ph.D., Hedy Migden, M.D.; Albany College of Pharmacy, Albany, NY; Altamont Internal Medicine and Pediatrics, Altamont, NY.

PURPOSE: Pharmaceutical manufacturer assistance programs (PMAPs) can provide medications to qualified patients who are unable to afford prescription drug therapy. Current literature has reported success of pharmacist-coordinated assistance programs in decreasing hospital costs in hospital-based ambulatory care or specialty clinics. Our study assessed the effect of incorporating PMAPs into clinical pharmacy services in a private ambulatory care setting and reports cost savings for patients.
METHODS: Patients were prospectively evaluated for eligibility into PMAPs by the clinic pharmacist from March 2001 through March 2002. A universal intake form was created to simplify the enrollment and reapplication process. The number of patients enrolled, patient demographics, medication dollar

value saved by the patient, the most commonly utilized programs by drug class, and time required by the pharmacist was recorded during the study period.
RESULTS: A total of 44 patients were enrolled into 22 PMAPs most commonly providing antihypertensives, antidepressants, antilipemics, proton pump inhibitors, and antidiabetic agents. The average patient age was 65.7 ± 17.6 and 80% of patients were female. There were 115 medications processed and the annual cost savings to patients was $48,581. The time required by the clinic pharmacist to process each medication, including initial enrollment and reapplications, was estimated at 1 hour per year.
CONCLUSION: Incorporating pharmaceutical manufacturer assistance programs into clinical pharmacy services in a private practice setting can decrease patient expenses in a time efficient manner.

371. Processing fee justification for medication assistance programs. *David M. Hachey, Pharm.D., BCPS;* Idaho State University, Pocatello, ID.

PURPOSE: Clinic and hospital-based patient assistance programs exist which support financially indigent patients in applying to pharmaceutical company sponsored medication assistance programs (MAP). Processing applications and dispensing medications to patients is time consuming and usually provided at no charge to patients. However, with the extensive time involved for managing these programs for many patients, clinics and hospitals are attempting to justify charging processing fees to patients to offset the cost of running a MAP. We set out to determine if practitioners who process applications for patients charge a fee and exactly how many applications they process monthly.
METHODS: A survey was administered electronically to the Ambulatory Care Pharmacy Research Network (AmCare PRN) asking practitioners who are involved with MAP if a dispensing fee was charged and if so, how much. They were also asked how many applications they processed monthly. The mean and median were calculated.
RESULTS: There were 32 responses. Six programs charged a processing/dispensing fee and 26 did not. For those that charged a fee, $5 was the average fee and the mean applications processed per month was 488 (range 100-1000; median 230). Those that did not charge a fee processed an average of 42 applications per month (range 4-200; median 25).
CONCLUSIONS: The majority of survey respondents who run MAPs do not charge an application processing/dispensing fee. However, those that do charge a fee, process, on average, a larger number of applications per month.

372. Outcomes associated with diabetes management services provided by pharmacists in a family medicine center. *Melissa M. Blair, Pharm.D.*, Andrea M. Wessell, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate the effect of pharmacist-provided diabetes management and education on glycemic control in patients at a Family Medicine Center.
METHODS: Patients were referred to pharmacists for diabetes management services. Patient contact occurred during clinic visits or over the telephone. Glycemic control, as measured by glycosylated hemoglobin (HbA_{1c}), was measured prior to, and at six months after the initiation of this service. Cost avoidance comparators, based on those found in the literature were calculated for those patients with a 1% reduction in HbA_{1c}. In patients with a > 1% increase in HbA_{1c}, charts were reviewed to determine reasons for worsened glycemic control.
RESULTS: Ninety-six patients were seen for diabetes management over a six-month period of time. Of these 69 (71%) had HbA_{1c} at baseline and follow-up. The average HbA_{1c} decreased 1% (9% versus 8%). Twenty-six patients (38%) experienced ≥ 1% reduction, 49% had no change, and 13% had a ≥ 1% increase in HbA_{1c} over six months. Based on an estimated savings of $820 for a 1% decrease in HbA_{1c}, total cost avoidance was calculated to be $21,320. Reasons for HbA_{1c} increases included: non-adherence to therapy or follow-up and inadequate treatment.
CONCLUSIONS: In a short period of time, pharmacist-provided diabetes management improved glycemic control with potential cost savings. Non-adherence, regardless of the underlying reason, remains a significant barrier to improvement in diabetes care.

373. The effect of setting on patient perceptions of a pharmacist-administered immunization program. Elizabeth W. Blake, Pharm.D., *Melissa M. Blair, Pharm.D.*, Kenneth W. Kenyon, Pharm.D., Kirsi M. Hearon, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To compare patient perception of and satisfaction with an adult immunization program administered by pharmacists in a pharmacy versus clinic setting.
METHODS: Over the past two years, pharmacists have administered immunizations during influenza season in patient care rooms of the Family Medicine Center. In 2001, the service was moved into the pharmacy. Pharmacy employees performed all aspects of the immunization program including: patient registration, shot provision and education, documentation, and billing. After several months, immunized patients were contacted by telephone and asked to respond to a 10-item Likert scale survey. Two attempts were made to contact each patient. Survey results were then compared to results from a previous survey administered when the service was provided in the clinic setting and were analyzed using chi-square.
RESULTS: One hundred thirty-three patients (43%) completed the survey. More respondents (40% vs. 13%) recalled that a pharmacist had administered the immunization than previously (p=0.0002). More respondents (63% vs. 41%) also felt comfortable with community pharmacists administering vaccinations (p=0.0047). Patient perceptions regarding qualifications of health care professionals to administer vaccines showed increased patient perception of pharmacists as immunizers (p=0.0001). Response rates concerning appropriate information given, comfort level with immunizer, and preference for immunizer to provide vaccines again did not significantly change from the previous survey.
CONCLUSIONS: By moving the immunization service into the pharmacy, more patients realized that a pharmacist provided their immunization, and patient perceptions regarding pharmacists as immunizers significantly improved. This demonstrates the importance of location in the provision of pharmacy services at this institution.

374. Contribution of the clinical trials section of the pharmaceutical services, to the rationalization of the medication circuit at Coimbra's University Hospitals. *José A. L. Feio, Pharm.D.,* Francisco Machado, Pharm.D., Artur Rebelo, Pharm.D., Maria A.L. Monteiro, Pharm.D., Maria L. Lemos, Pharm.D., Maria A. Martins, Pharm.D., Rufino Silva, M.D., Odete S. Isabel, Pharm.D.; Coimbra's University Hospital, Coimbra, Portugal.

PURPOSE: The pharmaceutical services of Coimbra's University Hospitals (HUC) started, in 1998 a clinical trial section. This section developed internal protocols related to prescription, distribution, preparation, administration and information making the medication circuit safer, more rational and efficient. The objective is to analyze the contribution of the clinical trials section of the HUC to the rationalization of the verteporfin circuit.
METHODS: A protocol in which the clinical trials section participated was selected. The medication, verteporfin, concluded the study and once approved its introduction in the hospital formulary was treated with the protocol procedures.
RESULTS: The circuit of the medication established for the trial, which contemplated an active intervention of the pharmacist in all stages (including preparation), was maintained after the introduction of the verteporfin in the hospital. Between April and August of 2001, 28 patients were included (52% men), average age of 71,4 and 52 treatments were performed. The medication is prepared in the vertical flow chamber in the pharmaceutical services and monitored by pharmacists until administration. $46,977 U.S. dollars were spent, 21% less than expected.
CONCLUSIONS: The implanted circuit of verteporfin during the protocol was followed after the introduction in the hospital and proved to be safe, efficient and rational.

375. Impact of pharmacist-conducted patient education and counseling. *Lynnette R. Klaus, R.Ph., Pharm.D. candidate*; Providence Portland Medical Center, Portland, OR.

PURPOSE: The Patient Safety Team at Providence Portland Medical Center (PPMC) identified the need for improved continuity of care as inpatients are discharged and transitioned to the outpatient setting. A pilot study was recommended to assess the efficacy and impact of having a pharmacist involved in the discharge process.
METHODS: Patients on the respiratory care unit at PPMC between May 7 and June 14, 2001 were chosen for the pilot study. Patients selected for counseling were identified via predetermined criteria based on the population statistics of patients admitted to the respiratory care unit. The pharmacist initiated interventions to improve continuity of care, reduce potential adverse events and medication errors, and to provide patient education. The economic impact of the interventions provided by the pharmacist was evaluated along with patient, physician and nursing satisfaction.
RESULTS: Seventy-two patients were evaluated and counseled by the clinical pharmacist with 120 interventions performed. A total cost savings of $10,130 was calculated using ASHP's CliniTrends for the interventions conducted by the clinical pharmacist. Satisfaction surveys distributed had a response rate of 100%, 67% and 40% from the physicians, nurses and patients, respectively, with a response in favor of having a pharmacist involved in the discharge process.
CONCLUSION: The clinical pharmacist had a positive impact on the provision of care for inpatients being transitioned to the outpatient setting. The outcome measures of patient, nurse and physician satisfaction were found to positively advocate the benefit of a clinical pharmacist providing discharge counseling.

376. Development of a comprehensive primary care clinical pharmacy service. *Cristina D. Gray, Pharm.D., BCPS*; Dwight D. Eisenhower VA Medical Center, Leavenworth, KS.

PURPOSE: To develop a clinical pharmacy service within a multi-disciplinary specialty/primary care clinic in order to 1) provide comprehensive care to veterans, 2) increase opportunities for student training, 3) increase physician availability for more complex visits, and 4) reduce drug costs and enhance formulary compliance.

METHODS: A residency trained Pharm.D. was hired at the time the clinic was developed in 1996 as well as two nurses, one dietitian, one social worker, four physicians, and two clerks.
RESULTS: The clinical pharmacy service continues to be active, with an average of twelve patients per day seen by the clinical pharmacist. The variety of disease states co-managed by the clinical pharmacist has expanded over time. Services provided include monitoring of all anticoagulation patients and interim management of lipid disorders, hypertension, congestive heart failure and diabetes between annual physician visits. One ambulatory care clerkship for Pharm.D. students is provided each month to the local universities. In addition, there is ongoing medication evaluation of all patients to reduce polypharmacy, drug costs, and improve medication adherence. Outcome measures evaluated to date include percent compliance of monthly laboratory monitoring for anticoagulation patients (increased from 85% to 98%), and drug cost (sustained reduction of 14% per patient per year).
CONCLUSION: Provision of daily clinical pharmacy services within the primary clinic has been successfully initiated and maintained over a six-year period. The arrangement allows for close communication and collaboration with the team members and continuity of care for patients.

377. Impact of clinical pharmacy services on a Cuban pediatric hospital. *A. Martinez Sanchez, Ph.D.*, De la Torre A. Rodriguez, B.Sc.Pharm., Alina de las Mercedes Martinez-Sanchez; University of Oriente; South Pediatric Hospital, Santiago de Cuba, Cuba.

PURPOSE: To evaluate the impact of the activity of the clinical pharmacy in the identification, solution and prevention of drug-related harm.
METHODS: Retrospective review of pharmacotherapy profiles open to patients hospitalized during the year 2001 in the Pharmacy Services Southern Pediatric Hospital of Santiago de Cuba, Cuba, it is a pediatric hospital of 329 beds, a clinical pharmacist for the whole hospital.
The pharmacy report activities are analyzed taking into account the following markers:
1. Drug interactions: with regard to implication for the results of the pharmacotherapy of the patient
2. Drug adverse reaction: (demonstration through Naranjo's Algorithm)
3. Pharmacy interventions.
4. Information to patients and health professionals about diseases and treatments.

RESULTS: A total of 29 pharmacotherapy profiles were analyzed. 15 medical interventions are detected of these 50% harmful and 33% not justified. 42 adverse drug reactions are detected 29% possible, 21% probable and 26% defined. 87 pharmacy interventions are carried out consisting in change of treatment. Eight seminars and three lectures are imparted to 18 health professionals of which three with B.A. in Nursing and 15 doctors, the topics being: treatment of the giardiasis, drug adverse reactions, drug interactions and uses of oftalmological drops. 13 patients received information about medications, the main pharmacological groups were: analgesic, antiparasitic and inhaled anti-asthmatic.
CONCLUSIONS: The results obtained show the importance of the existence of the clinical pharmaceutical services in Cuban pediatric hospital and its utility in the protections against drug-related harm that endanger the achievement of the optimal results of the pharmacotherapy. These ideas suggest the necessity that the clinical pharmaceutical services should be given in a continuos way to promote the safe and effective drug treatment for patients.

378. Implementation of an asthma point of care program in a chain pharmacy. *Magaly Rodriguez de Bittner, Pharm.D., BCPS*, Jennifer L. Jefferson, Pharm.D., Mona G. Tsoukleris, Pharm.D., BCPS, Tom Johnson, R.Ph, Gary Wirth, R.Ph., M.B.A., Annissia N. Janifer, Pharm.D.; University of Maryland; Giant Pharmacy, Baltimore, MD.

PURPOSE: Determine the feasibility of an asthma point of care program at a chain-pharmacy and improve asthma management through pharmacists' interventions.
METHODS: Patients receiving an asthma medication during the study period were instructed to see the pharmacist. Pharmacists obtained informed consent and used a standardized questionnaire and documentation form to record patient information. Pharmacists evaluated asthma control, medication use, inhaler technique, ability to identify rescue and controller medications, and existence of an action plan. Physicians were contacted with suggested interventions.
RESULTS: Seventy-five patients were program candidates, 62 provided informed consent. Fifty-three percent of patients had asthma, 75% noted bothersome asthma symptoms, 31.6% used a “quick relief” inhaler more than 2/week, 17.1% woke up at night more than 2/month and 40.8% refilled the quick relief inhaler more than 2/year. Eighteen percent identified controllers as their “quick-relief” inhaler, 38% used the inhaler incorrectly, and 64.5% had no action plan. Pharmacists intervened in 89% of cases needing intervention. An average of 5.1 minutes was required to collect data and make interventions. Lack of time and incentive were barriers to the program. Pharmacists and patients were satisfied with the service.
CONCLUSIONS: An asthma point of care program is feasible in a chain-pharmacy with some modifications. We found that a large number of patients did not identify their medications correctly, have adequate asthma control, use inhalers correctly or have an action plan. Modification of the service is in process to allow expansion of the service.

379. Health care provider survey of clinical pharmacy services in a family medicine clinic. *Sara B. Jutte, Pharm.D.*, Melissa M. Blair, Pharm.D., Kelly R. Ragucci, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To survey health care providers concerning the utilization and helpfulness of current clinical pharmacy services and to assess interest for expansion of pharmacy services in a Family Medicine Clinic.
METHODS: A one-page survey was designed and distributed through an internal mail system to nineteen health care providers: 17 physicians, 1 nurse practitioner, and 1 physician's assistant. Providers were instructed to anonymously return surveys to a clinical pharmacist's mailbox. If surveys were not returned, the provider was sent the survey again to increase response rate.
RESULTS: Fourteen of the nineteen (74%) health care providers returned surveys. Currently, the most utilized services were: anticoagulation (93%), diabetes (79%), asthma (57%), financial assistance (57%), and medication education (57%). Ninety-one percent of the providers found pharmacy services to be either helpful or very helpful. In addition to the above services, providers were interested in expanding pharmacist involvement in: smoking cessation (57%), medication management (57%), congestive heart failure (50%), nutrition (50%), and pain management (50%). Increased pharmacist participation was also desired in the areas of research and herbal remedies. The only area of concern regarding pharmacy services was related to duplication of patient education with the clinic's diabetes counselor.
CONCLUSIONS: A variety of clinical pharmacy services are currently utilized by health care providers and are perceived to be beneficial. In addition, several areas for expansion of services were identified. This information will enable clinical pharmacists to prioritize involvement in the Family Medicine Clinic.

380. Use of personal digital assistant to document primary care clinical pharmacy services. *Elizabeth A. Chester, Pharm.D., BCPS*, Rachana J. Patel, Pharm.D., Timothy J. Hartman, Pharm.D., BCPS; Kaiser Permanente, Aurora, CO; Kaiser Permanente, Denver, CO; Pfizer Pharmaceuticals Group, Parker, CO.

PURPOSE: Design and pilot a handheld computerized system for Primary Care Clinical Pharmacy Services (PCCPS) to facilitate the documentation of daily activities and describe their value to the organization.
METHODS: A clinical pharmacy documentation tool (PharmDoc) was developed for personal digital assistants (PDA, Handspring VisorPro) using ThinkDB software. From January to March 2002, seven primary care clinical pharmacists and clinical pharmacy specialists documented all daily activities (encounters) including patient care activities, consultations, administrative activities, and cost avoidance.
RESULTS: During the 3-month period, the pilot team documented 3250 encounters. Eighty-four percent of encounters (n=2799) fell into the following categories: administrative time, hypertension, lipids, diabetes, headache, women's health, mental health, adverse drug reactions, gastrointestinal disorders, neurological disorders, and pain management. Seventy percent of clinical pharmacy staff interventions (n=1816) were categorized as adjusted dose/interval, changed medication, continued current therapy, reviewed/ordered labs, and started medication. Of 347 clinical pharmacy staff recommendations, 87% were accepted. Estimated annual cost avoidance totaled $213,238. The following categories accounted for more than 90% of costs avoided — headache, lipids, pain management, hypertension, gastrointestinal disorders, neurological disorders, mental health, diabetes, women's health, asthma/COPD, and men's health.
CONCLUSION: Use of PharmDoc allowed the pilot group to document a higher than expected number of encounters and highlighted the diverse practice of PCCPS. If we consider these seven clinical pharmacy staff members a representative sample and extrapolate this data to 25 staff members, our service could potentially document over 46,000 encounters and $3 million in cost avoidance annually.

381. Assessment of a patient management information system to track and monitor use of baseline laboratory guidelines. *Peter Massad, Pharm.D., MPH, BCPP*; Cape Cod and the Islands Community Mental Health Center, Pocasset, MA.

PURPOSE: This study documented use of a facility designed patient management information system to track the monitoring, and appropriateness of baseline laboratory and electrocardiogram results for initiating designated psychiatric modalities. These guidelines, termed “Best Practices Recommendations” were developed by the Pharmacy and Therapeutics Committee, and they were periodically updated as new knowledge became available.
METHODS: Laboratory records of 49 patients admitted between November 1 and May 31, 2002 to the Inpatient Unit were reviewed. Patients' current medication regimen, in-hospital course, and specific laboratory tests ordered were assessed for consistency with the recommendations. Feedback from

practitioners was then evaluated.
RESULTS: Laboratory tests were tracked in 49 patients and included clozapine (31%), divalproate (15%), lithium (9%), ziprasidone (10%), and carbamazepine (1%). A greater proportion of patients achieved clozapine in accordance with the guidelines versus the next most commonly prescribed agent on the list, divalproate. Use of the guidelines provided a tool for ongoing assessment of prescribing practices, and it generated ongoing feedback as to the positive influence its placed on prescribing behaviors.
CONCLUSION: Clozapine was the predominant medication prescribed and the most intensively monitored in accordance with the guidelines for the period studied. Use of the patient management information system assisted the ongoing feedback reporting, and permitted the clinical pharmacist to measure and improve the medical staff's compliance with this system. An unanticipated outcome was the concurrent feedback by the medical staff toward creating enhancements to the Best Practices Recommendations as prescribing experience and the knowledge of the latest literature became available.

382. Assessment and reduction of antipsychotic polypharmacy in a psychiatric treatment and rehabilitation facility. *Stephen M. Dolley, B.S., BCPP,* Kathleen P. Whitley, M.D., Christopher C. Kennedy, M.D.; Worcester State Hospital, Worcester, MA.

PURPOSE: Antipsychotic polypharmacy has become common practice in many psychiatric settings despite little in the literature to support this practice. JCAHO ORYX data for Worcester State Hospital, a psychiatric treatment and rehabilitation facility, have indicated a higher rate of antipsychotic polypharmacy when compared to both state of Massachusetts and national averages.
METHODS: Members of the hospital Psychiatric Performance Improvement Committee, composed of representatives from the Departments of Psychiatry and Pharmacy, sought to understand this phenomenon with the goal of substantiating use of these combinations if clinically indicated and reducing their use where appropriate. The committee developed a physician survey that for each specific case of antipsychotic polypharmacy asked the prescriber to answer questions regarding the rationale for the current antipsychotic polypharmacy regimen and knowledge of single agent trials prior to the initiation of antipsychotic polypharmacy.
RESULTS: Survey results were reported to and discussed with all members of the psychiatric staff. Prescribers were educated to increase their awareness of issues such as medication costs and the higher risks of side effects when prescribing these combinations. This poster will report results of the aforementioned survey. Comparative JCAHO ORYX data as well as cost savings associated with a reduction in the use of antipsychotic polypharmacy will also be discussed.
CONCLUSION: A multidisciplinary assessment of antipsychotic polypharmacy at a psychiatric treatment and rehabilitation hospital increased awareness of the proper use of these combinations among prescribers and impacted both the prescribing patterns and financial burden associated with these regimens.

383. A statewide program to increase medication access for indigent solid-organ transplant patients. *Marie A. Chisholm, Pharm.D., FCCP,* Bridgett D. Kendrick, C.Ph.T., Charlene J. Garrett, Herbert E. McGinty, B.S., Jeanie C. Turner, B.S., Joseph T. DiPiro, Pharm.D., FCCP; University of Georgia; Medical College of Georgia, Augusta, GA.

PURPOSE: Many solid-organ transplant (SOT) patients have inadequate prescription insurance and do not have the financial resources to pay for all of their medication needs. In recognition of this, many pharmaceutical manufacturers make their medications available for free, or at a reduced cost, through medication assistance programs. These programs are available to eligible patients who do not have access to essential medications by any other means. The Medication Access Program (MAP) assists patients in the enrollment process of these medication assistance programs and educates healthcare professionals about them.
METHODS: The MAP office has five employees, including two pharmacists. Georgia's SOT patients that are in need of medication assistance, or their physician, can contact the MAP office concerning the availability of medication assistance programs. MAP personnel instructs patients and healthcare personnel on the application process that is required by the pharmaceutical companies. MAP also serves as a liaison between the patient, physician, and the pharmaceutical companies. In a database, MAP personnel documents the number of patients served and the average wholesale price (AWP) of medications supplied through the program. Patients who used MAP's services, as of January 1999, were asked to complete a patient satisfaction survey.
RESULTS: From October 1999 to June 2002, MAP has assisted over 266 SOT patients in the enrollment into medication assistance programs, accounting for approximately $2.4 million (AWP cost) of medications. Approximately 51% of the $2.4 million represents immunosuppressant medications, the other 49% mostly represents that of cardiovascular, antimicrobial, and gastrointestinal medications. On the patient satisfaction survey, patients (n = 175) had a mean score of 95.2 ± 10.7 (highest achievable survey score was 100), indicating that MAP provided a valuable service to them.
CONCLUSION: The MAP program is successful in helping needy solid-organ transplant patients obtain medications, and patients are pleased with the services that the MAP program provides.

Student, Resident, Fellow Research in Progress

These papers describe original research by students, residents, and fellows in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, and pharmacoepidemiology 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.

384. Pilot study of the correlation and clinical agreement of a portable coagulation monitor for point-of-care patient management (CoaguChek S®). *Tara D. Storjohann, Pharm.D.,* Holly S. Rickman, M.S., Pharm.D., Jennifer L. Bolding, Pharm.D.; Central Arkansas Veterans Healthcare System, Little Rock, AR.

385. Use of bivalirudin in patients undergoing percutaneous coronary interventions. *Estela M. Trimino, Pharm.D.,* Janelle M. Berg, Pharm.D., BCPS; Mercy Hospital, Miami, FL.

386. Influence of polymorphism on the β_1 and β_2 adrenergic receptor genes in obesity. *Cathy D. Crumel, Pharm.D.,* Jianwei Wang, M.D., Hardesh Garg, M.D., James Sylvester, Ph.D., John J. Lima, Pharm.D.; Nemours Children's Clinic; University of Florida, Jacksonville, FL.

387. Cytotoxicity of cisplatin bound to human serum albumin compared to free cisplatin. *Susanne E. Liewer, Pharm.D.,* Aimee K. Bence, Ph.D., Melody Ryan, Pharm.D., CGP, BCPS, Hetal S. Patel, Pharm.D., Val R. Adams, Pharm.D., BCOP; University of Kentucky, Lexington, KY.

388. A quality assessment study of adherence with health plan employer data information set criteria for blood pressure control in a managed care population. *Tanya M. Romain, Pharm.D.,* Andrea M. Heaberlin, Pharm.D., Rosalie P. Patel, Pharm.D., Barbara J. Zarowitz, Pharm.D., BCPS, FCCP; Henry Ford Health System, Detroit MI.

389. Inappropriate metformin use among hospitalized patients in an urban, tertiary care institution. *Elizabeth Knapp, B.Sc.,* Peter Dumo, Pharm.D.; Wayne State University; Harper University Hospital, Detroit, MI.

390. Inhaled glucocorticoid effects on stiffness index and t-scores in female patients. *Alicia B. Forinash, Pharm.D.,* Stephanie L. Evans, Pharm.D., Robert C. Baker, Pharm.D., John M. Burke, Pharm.D., FCCP; St. Louis College of Pharmacy; Family Medicine of St. Louis, St. Louis, MO.

391. Pharmacist intervention in prevention and treatment of glucocorticoid-induced osteoporosis at a family practice residency program. *Sarah F. Hutton, Pharm.D.,* Peter G. Koval, Pharm.D., BCPS; Moses Cone Family Practice, Greensboro, NC.

392. Pharmacist intervention in lipid management at a family practice residency program. *Sarah F. Hutton, Pharm.D.,* Peter G. Koval, Pharm.D., BCPS; Moses Cone Family Practice, Greenboro, NC.

393. Retrospective analysis of adverse events associated with long-term antibiotic therapy for serious Gram-positive infections. *Agatha C. Graham, Pharm.D.,* Renee-Claude Mercier, Pharm.D., Louis Achusim, Pharm.D., Manjunath P. Pai, Pharm.D.; University of New Mexico Health Sciences Center, Albuquerque, NM.

394. Under-utilization of inhaled corticosteroids in Medicaid asthmatic patients. Melanie A. Dodd, Pharm.D., BCPS, *Bijal M. Shah, B.S.,* Gireesh V. Gupchup, Ph.D., Joe R. Anderson, Pharm.D.; University of New Mexico, Albuquerque, NM.

395. Assessment of post-transplant osteoporosis in pre-menopausal and post-menopausal renal transplant recipients. *Bharati Bhardwaja, Pharm.D.,* Kathleen M. Tornatore, Pharm.D., Robert J. Fountaine, Pharm.D., Jennie Hom, M.D., Rocco Venuto, M.D.; State University of New York; University at Buffalo; Erie County Medical Center, Buffalo, NY.

396. Assessment of leukocyte function utilizing ^{18}F-fluorodeoxyglucose. *Dmitri Mayer, B.S.,* Edward M. Bednarczyk, Pharm.D., Lynn M. Kaczmarek, B.S., Joseph W. Vilani, M.S., Hani A. Nabi, M.D., Ph.D.; State University of New York, University at Buffalo, Buffalo, NY.

397. Intensive glucose control and the incidence of infection in critically ill patients receiving parenteral nutrition. *Eric G. Sahloff,* Steven J. Martin, Martin Ohlinger, David Richards; University of Toledo; St. Vincent Mercy Medical Center, Toledo, OH.

398. Amiodarone compliance with the 2000 advanced cardiac life support guidelines. *Jamie P. Reuter, Pharm.D.,* James Kirby, R.Ph., Steven E. Pass, Pharm.D., BCPS, Michelle L. Dusing, Pharm.D., BCPS; University of Cincinnati, Cincinnati, OH.

399. Cancer-related fatigue assessment and its impact on prescribing habits. *J. Michael Vozniak, Pharm.D.,* Val R. Adams, Pharm.D., BCOP, David Eckman, Pharm.D., Courtney Smith, Pharm.D.; University of Kentucky, Lexington, KY.

400. Determination of bleeding events associated with percutaneous coronary intervention. *Sallie K. Young, Pharm.D.,* Ann K. Wittkowsky, Pharm.D., CACP, Kathleen A. Stringer, Pharm.D., FCCP, Howard C. Herrmann, M.D., Sarah A. Spinler, Pharm.D., FCCP; University of the Sciences in Philadelphia, Philadelphia, PA; University of Washington Medical Center, Seattle, WA; University of Colorado Health Sciences Center, Denver, CO; University of Pennsylvania, Philadelphia, PA.

401. Factors associated with calcineurin-inhibitor induced renal insufficiency. *Cynthia B. Gierwatowski,* Kenneth E. Thummel, Ph.D., Connie L. Davis, M.D., Amy Dowling, Ph.D., Mary F. Hebert, Pharm.D.; University of Washington, Seattle, WA.

402. Patient characteristics and medication-related factors in the type 2 diabetic population: are they related to A_{1c} and medication adherence measures? *Kristal L. Williams, Pharm.D.,* Peggy S. Odegard, Pharm.D., BCPS, CDE, Shelly L. Gray, Pharm.D., BCPS, M.S., Alvin Goo, Pharm.D., BCPS, CDE; University of Washington; Harborview Medical Center; Seattle, WA.

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.

403. Aventis Infectious Diseases Fellowship: The effects of didanosine formulations on the pharmacokinetics of amprenavir. *Angela A. Giovanniello, Pharm.D.,* Mark J. Shelton, Pharm.D., Denise Cloen, R.N., Charles S. Berenson, M.D., Kim Keil, Ross G. Hewitt, M.D.; Metcare, New York, NY; GlaxoSmithKline, Research Triangle Park, NC; University at Buffalo, Buffalo, NY; Western New York Healthcare System, Buffalo, NY.

PURPOSE: To determine the effects of didanosine (ddI) (buffered and enteric-coated) on amprenavir (APV) pharmacokinetics (PK), which is more soluble at acidic pH.
METHODS: The study was conducted in healthy volunteers during two periods, each separated by 11 days wash-out. APV (4x150-mg capsules BID) was given on days 1-4 and days 15-18. PK was evaluated during the following, sequential treatments (all fasting): APV alone (day 3), APV with 2x200 mg ddI buffered tablets (day 4), APV 1-hour prior to buffered ddI (day 17), and APV with 1 x 400 mg ddI enteric-coated capsule (day 18). Plasma was collected 0, 1, 2, 3, 4, 6, 8, and 12 hours after dosing and assayed for APV using HPLC. Non-compartmental PK parameters were determined and reported as geometric mean ratio (GMR) with 90% confidence interval for each treatment/control (day 3).
RESULTS: 16 subjects completed the study. With regard to $AUC_{0\text{-}12h}$, all study treatments met bioequivalence standards, with mean changes of ≤ 10%. For concurrent, buffered ddI, GMR for C_{max} and $AUC_{0\text{-}12h}$ were 0.85 (0.7308, 0.9970) and 0.97 (0.8760,1.0810), respectively. For staggered ddI administration, GMRs (same parameters) were 1.05 (0.9383, 1.1674) and 1.08 (0.9917, 1.1746). For concurrent enteric-coated ddI, GMRs were 0.93 (0.7814, 1.0993) and 0.94 (0.8223, 1.0789). No differences were observed in C12 hours.
CONCLUSIONS: Since APV virologic response is better related to average plasma concentration compared to C_{max}, the minor PK changes seen with concurrent ddI are unlikely to be clinically significant. Therefore, APV capsules may be dosed concurrently with both buffered ddI and enteric-coated ddI in the fasting state.

404. Merck Cardiovascular Fellowship: Effect of sildenafil on hemodynamics and resistance vessel function. *John M. Dopp, Pharm.D.,* Alexei V. Agapitov, M.D., William G. Haynes, M.D., Bradley G. Phillips, Pharm.D.; University of Iowa, Iowa City, IA.

PURPOSE: Sildenafil, a phosphodiesterase-type 5 (PDE-5) inhibitor, is an effective therapy for erectile dysfunction. If PDE-5 is present in other vascular tissues, sildenafil may positively affect hemodynamics and vasodilatation by enhancing the actions of nitric oxide (NO). We tested the hypothesis that sildenafil would enhance endothelium-dependent and –independent vasodilatation in resistance vessels.
METHODS: We prospectively studied 10 middle-aged, healthy male volunteers (mean age 43.3 ± 2.4 years), randomized to receive 100 mg sildenafil and placebo in a double-blind fashion on two separate study visits. Hemodynamics (blood pressure, heart rate, cardiac output and stroke volume) and plasma catecholamines were measured at baseline and 60 minutes after study drug administration. Forearm resistance vessel responses to increasing doses of intra-brachial acetylcholine (ACh, an endothelium-dependent dilator) and sodium nitroprusside (SNP, an endothelium-independent dilator) were measured using venous occlusion plethysmography.
RESULTS: Area under the curve (AUC) for percent decrease in forearm vascular resistance (FVR) from baseline was 727 ± 101 and 712 ± 133 during ACh (3,10,30 µg/minute) following sildenafil and placebo, respectively. AUC for percent decrease in FVR from baseline was 888 ± 68 and 881 ± 72 during SNP (1, 3, 10 µg/minute) following sildenafil and placebo, respectively. Mean arterial pressure was unchanged following sildenafil administration. Heart rate increased slightly following sildenafil and was unchanged after placebo (p=0.02). Cardiac output and stroke volume were unchanged following sildenafil and placebo. Plasma catecholamines increased 58 ± 19 % following sildenafil and 20 ± 19% following placebo (p=0.003).
CONCLUSIONS: Sildenafil did not improve forearm resistance vessel endothelium-dependent or –independent vasodilatation, nor did it significantly impact hemodynamics in healthy, middle-aged men. Increases in sympathetic drive may mask changes in hemodynamics and forearm resistance vessel NO-mediated vasodilatation.

405. Merck Pharmacoeconomics and Outcomes Fellowship: Is use of an NSAID associated with first occurrence of congestive heart failure? A prospective case-control study. *Brian J. Gates, Pharm.D.,* Steven M. Setter, Pharm.D., D.V.M., David A. Sclar, B.Pharm., Ph.D., Linda M. Robison, MSPH; Washington State University, Spokane, WA.

PURPOSE: The present study was designed to discern: (1) the relationship between exposure to an NSAID and first (incident) admission to hospital for congestive heart failure (CHF); (2) exposure to an NSAID among incident and prevalence cases of CHF; and (3) the relationship between NSAID half-life and admission for CHF.
METHODS: Prospective case-control study (n=343; ≥ 50 years). Cases (n=157; incident=100; prevalence=57) were patients admitted to hospital with a primary diagnosis of CHF. Controls (n=186) were patients admitted to hospital without CHF (or history of CHF). Exposure was defined as use of an NSAID for ≥ 1 week in the month prior to hospital admission. Data were collected via a structured interview. Multiple conditional logistic regression was used to generate odds-ratios and 95% confidence intervals (CIs), and to adjust for selected demographic and clinical factors. The a priori level of significance was set at p≤0.05.
RESULTS: Use of an NSAID for ≥ 1 week in the month prior to hospital admission was associated with a 21% increase (OR=1.21, CI=1.08-1.64; p≤0.05) in the odds of admission for CHF (incident case). Prevalence CHF cases were 2.74 times less likely (OR=0.365, CI=0.149-0.895; p≤0.05) to have used an NSAID for ≥ 1 week in the month prior to hospital admission relative to incident cases. NSAID half-life was not found to influence hospital admission for CHF.
CONCLUSION: Use of an NSAID is associated with increased probability of first (incident) admission for CHF. Use of NSAIDs in persons ≥ 50 years warrants caution, and assessment of concomitant risk-factors for CHF.

406. Ortho-McNeil Infectious Diseases Fellowship: Pharmacokinetic characteristics of a protease inhibitor based salvage antiretroviral treatment regimen in HIV-infected adults. *Heather E. Wynn, Pharm.D.,* Peter L. Anderson, Pharm.D., Courtney V. Fletcher, Pharm.D.; University of Minnesota, Minneapolis, MN; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: HIV infected persons who are highly experienced with combination antiretroviral therapies are common in the clinical setting. Suppression of viremia is often difficult to achieve and maintain. Failure to suppress viral replication may in part be due to suboptimal antiretroviral drug exposure in heavily pre-treated patients. To address this hypothesis, our primary objective is to determine the steady state pharmacokinetic parameters of amprenavir (APV) 600 mg PO q12h and lopinavir/ritonavir (LPV/RTV) 400/100 mg PO q12h when used in combination as part of a salvage antiretroviral treatment regimen.
METHODS: Subjects with 2 or more treatment regimen failures starting APV and LPV/RTV based salvage therapy will be recruited. Subjects will have no active opportunistic infections and plasma HIV-1 RNA ≥ 10,000 copies/mL on two consecutive occasions. At week 0, blood will be drawn for viral genotype, viral phenotype, viral fitness test, and human DNA. At week 2, plasma will be collected over 12 hours for APV, LPV and RTV. Noncompartmental methods will be used to characterize APV, LPV and RTV plasma pharmacokinetics. Follow-up study visits for routine laboratory blood work, CD4 counts, HIV-1 RNA, and random APV, LPV, and RTV plasma samples will occur at weeks 4, 8, 12, 16, 20, and 24. Medication adherence will be monitored at each visit through subject interview and a self-administered questionnaire.
RESULTS: A total of 14 subjects will be recruited. The following plasma pharmacokinetic parameters will be determined for APV, LPV and RTV: C_{max}, T_{max}, C_{min}, V/F, $t_{1/2}$, CL/F, and $AUC_{0\text{-}12}$. Descriptive statistics will be reported for all pharmacokinetic data. Exploratory analyses to look for relationships between metrics of drug exposure and changes in HIV-1 RNA and CD4 count are planned using linear regression.
CONCLUSIONS: By characterizing the steady state pharmacokinetic parameters of APV, LPV, and RTV as part of salvage therapy and exploring protease inhibitor exposure-response relationships in treatment experienced HIV-infected persons, we may begin to identify ways to optimize dosing and

improve response and durability of future salvage antiretroviral treatment regimens.

407. Roche Transplantation Fellowship: CYP3A4*1B as a predictor for tacrolimus dosing in liver transplant patients. *Kareem Albakairy,* Christine Formea, Tuan Luu1, Heather Myers, Son Nguyen, Valerie Green, Shiro Fujita, Alan Hemming, Willem Van der Werf, Alan Reed, Richard Howard, Janet L. Karlix; University of Florida, Gainesville, FL.

BACKGROUND: CYP3A4 is an important drug metabolism enzyme in the transplant population because it facilitates the metabolism of cyclosporine, tacrolimus, and sirolimus. Up to 40-fold inter-individual differences have been reported in the activity of CYP3A4. Recently, a transition mutation [A>G] in the 5'-promotor region in the CYP3A4 gene has been described. There are conflicting reports on the clinical relevance of this variant form of CYP3A4 [CYP3A4*1B]; however, it has been described as being associated with lower metabolism requirements. We hypothesized that the presence or absence of CYP3A4*1B would explain the large variability in CYP3A4 activity and thus impact tacrolimus dosing requirement in transplant patients.
PURPOSE: To determine the role of CYP3A4*1B on tacrolimus dosing in stable liver transplant recipients.
METHODS: Liver transplant recipients followed as outpatients at our center were stratified according to tacrolimus dose required to maintain target concentrations [5-15 ng/ml]. Genomic DNA was isolated from whole blood via Puregene DNA isolation kit [Gentra systems, Minneapolis, MN]. Genotype was determined via restriction fragment length polymorphism [RFLP] analysis.
RESULTS: This study included 45 liver transplant recipients whose tacrolimus dose was stable for at least 4 weeks, with a stable FK level [5-15 ng/ml] and who were on no drugs known to interact with tacrolimus. There were 31 wild type (AA) patients and 14 variant (3 homozygous and 11 heterozygous). The tacrolimus dose was 0.041 mg/kg/day in the variant group vs. 0.052 mg/kg/day in the wild type group. In low FK dose grouping, [0.03 mg/kg/d], 4/31[13%] were wild type vs. 6/14 [43%] variant. In high dose stratification, [>0.1 mg/kg/d] there were 0 variants. These data suggest that this SNP may be a predictor for low metabolizers.
CONCLUSION: The recently identified polymorphism [CYP3A4*1B] may be a predictor for low CYP3A4 activity and tacrolimus requirements in liver transplant recipients.

408. Amgen Biotechnology Research Award: Trans vivo delayed type hypersensitivity response to hepatitis B surface antigen in vaccinated patients awaiting lung transplantation. *Mary S. Hayney, Pharm.D., BCPS,* William J. Burlingham, Ph.D., Frances L. Pelsue, Renee M. Fohl, Robert B. Love, M.D.; University of Wisconsin, Madison, WI.

PURPOSE: Patients with end-stage lung disease awaiting lung transplantation are candidates for hepatitis B vaccination, but they have low rates of antibody response to the vaccine series. The objective of this study was to compare the hepatitis B vaccine-induced cell mediated immune response to hepatitis B surface antigen (HBsAg) in patients awaiting lung transplantation to healthy controls. We hypothesized that cell mediated immunity would be similar between the two groups.
METHODS: Fifteen vaccinated healthy controls and five patients awaiting lung transplantation were enrolled. Human peripheral blood mononuclear cells (PBMC) were isolated for use in the trans vivo delayed type hypersensitivity (DTH) assay. PBMC alone and with antigen are injected into the footpad of an immunodeficient mouse causing a swelling that is an index of T cell sensitization. We estimated that a difference of $15x10^{-4}$ inches would be a clinically significant difference and the power to detect this difference is greater than 90%.
RESULTS: The healthy control group is younger than the patients awaiting lung transplantation. However, we found no difference in DTH swelling elicited by HBsAg or with tetanus toxoid (TT) used as a positive control.

	Healthy controls	Patients waiting transplant	p value
Age (years)	33.9 ± 2.4	46.3 ± 4.5	0.032
HBsAg ($x10^{-4}$ inches)	34.67 ± 4.3	28.75 ± 5.9	0.52
TT ($x10^{-4}$ inches)	15.67 ± 2.8	18.75 ± 9.4	0.77

CONCLUSION: Patients awaiting lung transplantation mount a DTH response to HBsAg that is similar to healthy controls in contrast to their markedly lower rate of antibody response. The role of cell mediated immunity in protection from infection requires further study.

409. Amgen Oncology Research Award: A novel antineoplastic agent with a unique mechanism of action. *Shewan M. Aziz, R.Ph., Ph.D., BCOP,* Vincent La Russa, Ph.D., Bennett Yu, M.D., Jay Schwab, R.Ph., BCNSP; Eastern Maine Medical Center, Bangor, ME; Tulane Medical Center, New Orleans, LA; Henry Ford Hospital, Detroit, MI.

PURPOSE: Due to the significant rise in percent mortality from neoplastic disease, much attention has been focused on identifying novel cellular mechanisms for pharmacological interventions in this disease therapy. Accordingly, one target for such interventions is the increase in cellular polyamine content, which derives cell transformation and cellular proliferation. However, pharmacological inhibition of polyamine synthesis (blocking ornithine decarboxylase activity with α-difluoromethylornithine) is unsuccessful in cancer treatment due to compensatory induction of polyamine transport. The purpose of this study is to use a novel polymeric conjugate of spermine (poly-SPM) that selectively blocks the polyamine transport system to demonstrate the potential therapeutic exploitation of this system in anticancer therapy.
METHOD: Human cancer cell lines used in this study were grown, subcultured, and maintained at 37°C in a humidified atmosphere according to previously reported methods. Polyamine transport and metabolism, and cellular cytotoxicity assays were conducted as described previously. Tumor xenografts were initiated by inoculating nude mice with human cancer cells injected subcutaneously under the flank of each mouse. The reduced polymeric glutaraldehyde conjugates of spermine was prepared as previously described by the author.
RESULTS: Poly-SPM was effective in blocking the influx of polyamines and exerting cytotoxicity in estrogen positive breast cancer (MCF-7) and colorectal cancer (LST174 and HT-19) cells. Similarly, poly-SPM reduced the active component of the polyamine transport system in anapestic human thyroid carcinoma (DRO90-1) cells. This inhibition persisted despite the removal of poly-SPM from the cell media. The concentration dependent cytotoxicity induced by poly-SPM in DRO90-1 coincided with a significant depletion of intracellular levels of all polyamines. Free polyamines failed to produce the same level of cytotoxicity, suggesting that the cytotoxic effect of poly-SPM cannot be simulated by the use of free polyamines. In contrast, in the same human cancer cell line, DFMO induced polyamine transport which was reversed and completely blocked in the presence of poly-SPM. In addition, DFMO failed to exert a cytotoxic effect and produced a modest decrease in the intracellular levels of all polyamines. Moreover, the combination of DFMO and poly-SPM produced a greater depletion of polyamine content than either agent alone. Finally, results of in vivo studies showed that treatment with poly-SPM significantly retarded the growth of DRO90-1 tumor xenograft in nude mice as compared to controlled nude mice.
CONCLUSION: Results of this study provide direct evidence that the pharmacological interruption of the polyamine transport system with poly-SPM provides a novel and an effective approach to cancer therapy. Unlike other antineoplastic agents, poly-SPM seems to be effective against several human cancer cell lines.

410. Amgen Oncology Research Award: NQO1*2 polymorphism is more frequent in nonsmall-cell-lung cancer tumors than matched normal nodes. Jill M. Kolesar, Pharm.D., Mark Vangel, Ph.D., Howard McLeod, Pharm.D., Adam Breunig, B.S., Judy A. Miller, B.S., Joan H. Schiller, M.D., David Johnson, M.D.; Eastern Cooperative Oncology Group; Washington University, Washington D.C.; University of Wisconsin, Madison, WI; Vanderbilt University, Nashville, TN.

Introduction: E3590 was a randomized, prospective trial of adjuvant radiation alone (Arm A) or radiation plus chemotherapy (Arm B) with etoposide and cisplatin in patients with resected II or IIIA NSCLC. NQO1 is a two-electron reductase, with a characteristic polymorphism (NQO1*2) that results in an inactive enzyme. Since NQO1 may be important in predicting chemosensitivity and toxicity, the influence of the NQO1*2 polymorphism on toxicity and overall survival in patients in E3590 was evaluated.
Methods: Genomic DNA isolated from primary lung tumor was evaluated for the NQO1*2 polymorphism by pyrosequencing, an automated sequencing method based on primer extension chemistry. Patients were designated as *1/*1, *1/*2, or *2/*2. Overall survival for these three groups was compared using Kaplan-Meier survival analysis with two-sided log rank tests. Results: There were 78 tumor samples available for analysis in Arm A, 54% of samples were *1/*1, 29% of samples were *1/*2, 16% of samples were *2/*2. There were 74 tumor samples available for analysis in Arm B, 55% of samples were *1/*1, 30% of samples were *1/*2, 15% of samples were *2/*2. In patients receiving radiation + chemotherapy (Arm B), NQO1 *2/*2 was a strong independent predictor of poor survival, with a median survival of 41.8 months for the *1/*1, 39.8 months for the *1/*2, and 16.2 months of the *2/*2. The median survival in patients receiving just radiation (Arm A) was 40.2 months for the *1/*1, 45.2 months for the *1/*2, and 53.4 of the *2/*2. The estimated hazard ratio comparing NQO1*2 in Arm B with NQO1*2 in Arm A was 3.6, with 95% confidence interval (1.4,9.2) p=0.028.
Conclusion: NQO1*2 predicts poor survival in NSCLC patients receiving radiation and chemotherapy. This genotype may help individualize cancer therapy, by predicting poor responders who may benefit from alternative therapies.

411. AstraZeneca Cardiovascular Research Award: Sympathetic regulation of monocyte TNF-α/IL-10 balance in impaired in severe heart failure. *Tien M.H. Ng, Pharm.D.,* Amy M. Vrana, B.S., Tom D. Sears, M.D.; University of Nebraska Medical Center, Omaha, NE.

BACKGROUND: The importance of the pro-inflammatory cytokine tumor necrosis factor (TNF)-α to the pathophysiology and prognosis of heart failure (CHF) has been recognized. Under normal physiologic conditions, TNF-α

production is counter-regulated by both interleukin-10 (IL-10) and sympathetic activation. A paradox exists in CHF as both norepinephrine (NE) and TNF-α are elevated, suggesting this negative feedback mechanism may be impaired, thus contributing to the pro-inflammatory state in CHF. The relationship between sympathetic activation and inflammatory cytokine balance in CHF has not been characterized. We hypothesized that attenuation of TNF-α production by NE in LPS-stimulated monocytes is diminished in CHF compared to healthy, age-matched volunteers.
METHODS: Monocytes were isolated via a standard Nycodenz method, from 12 CHF subjects (66 ± 12 y, NYHA FC 6 III, 6 IV, LVEF 20 ± 10%) and 14 healthy volunteers (66 ± 12 y). Isolated monocytes (1 x 10^6/mL) were incubated with LPS 100 ng/mL, LPS+NE 10^{-6} M or neither (control) for 4 hours. TNF-α and IL-10 production were determined by ELISA.
RESULTS: Basal TNF-α concentrations were higher in CHF patients than healthy subjects (6.3 ± 3.3 vs. 2.5 ± 2.6 pg/mL, p=0.004). Attenuation of TNF-α production by NE was diminished in CHF (-41 ± 17 CHF vs. -57 ± 9% healthies, p=0.01). Augmentation of IL-10 production by NE was also reduced in CHF (16 ± 18 CHF vs. 38 ± 23% healthies, p=0.012). Response of monocytes to NE was diminished to the greatest degree in NYHA FC IV patients compared to FC III and healthies for both TNF-α and IL-10 production (figure). There was a trend towards reduced IL-10 response in patients with LVEF ≤ 20% when compared to those with LVEF > 20% (7 ± 12 vs. 25 ± 20%, p=0.07).
CONCLUSIONS: Sympathetic counter-regulation of inflammatory cytokine response in monocytes appears to be reduced in moderate to severe CHF. Impairment is greatest in NYHA FC IV. This may be novel mechanism to explain increased expression of TNF-α in CHF. Future experiments to characterize the underlying mechanism are required.

412. Aventis Cardiovascular Research Award: Effect of grapefruit juice on digoxin pharmacokinetics in humans. *Robert B. Parker, Pharm.D.*, C. Ryan Yates, Pharm.D., Ph.D., Judith E. Soberman, M.D., S. Casey Laizure, Pharm.D.; University of Tennessee, Memphis, TN.

PURPOSE: Numerous studies demonstrate an interaction between grapefruit juice (GFJ) and drugs that are substrates for cytochrome P450 3A4 (CYP3A4). These investigations indicate that GFJ increases oral drug bioavailability via mechanism-based inhibition of intestinal CYP3A4. In addition, recent evidence suggests GFJ may also affect drug absorption via inhibition of the intestinal drug efflux transporter, P-glycoprotein (P-gp). To accurately characterize the interaction between GFJ and P-gp, it is necessary to use in vivo probes that interact with P-gp and not CYP3A4. Therefore, the purpose of this study is to determine the effects of GFJ on oral digoxin (a P-gp substrate not metabolized by CYP3A4) pharmacokinetics in normal healthy volunteers.
METHODS: Seven healthy non-smoking adult volunteers (4 male, 3 female) received 1.0 mg oral digoxin with water or GFJ in an unblinded, crossover study design with at least a 2 week washout between treatments. Before digoxin treatment, GFJ was administered 3 times daily for 5 days to maximize any effect on P-gp. Blood and urine were collected at various times for 144 hours after digoxin administration. Digoxin plasma and urine concentrations were determined by RIA and pharmacokinetic parameters determined by WinNonlin®.
RESULTS: Pharmacokinetic parameters are summarized below:

Parameter	Digoxin + Water (range)	Digoxin + GFJ (range)
$AUC_{(0\text{-}4\ hr)}$(ng•hour/ml)	8.4 ± 2.6 (5.3-11.9)	8.0 ± 1.5 (5.8-9.9)
$AUC_{(0\text{-}\infty)}$(ng•hour/ml)	61.0 ± 13.1 (39.7-83.8)	62.9 ± 14.2 (42.4-87.2)
C_{max} (ng/ml)	3.7 ± 1.7 (1.9-6.2)	3.1 ± 0.6 (2.0-3.8)
T_{max} (hour)	1.6 ± 1.2 (0.7-2.0)	2.0 ± 1.0 (1.0-4.0)
k_a ($hour^{-1}$)	3.0 ± 2.4 (0.5-6.6)	1.2 ± 1.0* (0.5-3.5)
T_{lag} (hour)	0.32 ± 0.12 (0.16-0.47)	0.53 ± 0.34* (0.09-0.94)
Half-life (hour)	38.0 ± 6.1 (31.5-46.1)	36.9 ± 4.0 (32.0-40.8)
CL_R (0-144 hour) (l/hour)	4.9 ± 1.7 (3.2-7.5)	5.3 ± 1.3 (3.8-7.0)

*p<0.05 compared to water phase by paired t-test; data are mean ± SD

CONCLUSIONS: 1) GFJ significantly reduced the rate of digoxin absorption which is opposite what would be expected with inhibition of intestinal P-gp transport; 2) On average, GFJ did not affect the extent of digoxin absorption although there was large interindividual variability in the response to GFJ (e.g., the effect of GFJ on C_{max} ranged from -45 to +41%); 3) GFJ did not affect systemic digoxin elimination; 4) Using digoxin as an in vivo probe, inhibition of intestinal P-gp does not appear to play an important role in drug interactions involving GFJ.

413. Aventis Cardiovascular Research Award: Effect of heart failure on myocardial P-glycoprotein expression. *J. Jason Sims, Pharm.D.*, Brien L. Neudeck, Pharm.D., Jennifer M. Loeb, B.S., Nicholas A. Wiegert, B.S.; University of Wisconsin, Madison, WI.

BACKGROUND: Heart failure is a complex of symptoms related to inadequate tissue perfusion that results in impaired quality of life, significant morbidity, and shortened life expectancy. There are multiple "protective" proteins that are synthesized in response to the stressful physiologic stimuli produced by heart failure. These often include proteins that are thought to help stabilize and repair cell damage. P-glycoprotein (PgP), encoded by the MDR1 gene and most commonly linked to drug transport, contributes to cellular protection against potentially toxic substances by extrusion of these substances out of cells. Interestingly, PgP has been found to be present and functional in myocardium. Thus, we hypothesize that PgP expression is increased in heart failure.
METHODS: Twenty-nine dogs were randomized to rapid-pacing induced heart failure (n=13) or unpaced sham operated control (n=16). Dogs were euthanized after 4 weeks of pacing at 250 beats per minute or 4 weeks of unpaced control. Left ventricular lateral wall myocardial samples were homogenized and prepared for protein analysis and RNA extraction. Total PgP protein was quantified using laser-induced fluorescence (Agilent 2100 Bioanalyzer). PgP and GAPDH mRNA expression was determined using semi-quantitative RT-PCR. RT-PCR data are presented as the normalized ratio of PgP/GAPDH.
RESULTS: RT-PCR revealed that heart failure increased mRNA expression of PgP (0.15 + 0.02 control versus 0.34 + 0.24 heart failure). However, heart failure did not alter the amount of PgP protein (0.14 + 0.07 µg/ml control versus 0.12 + 0.04 µg/ml heart failure).
CONCLUSIONS: Pacing induced heart failure increases p-glycoprotein mRNA expression. However, this increase did not alter the amount of total protein between control and heart failure. Thus, there appears to be a defect in the translation of p-glycoprotein during pacing induced heart failure. Therefore, an important cellular protection mechanism may be impaired during pacing induced heart failure.

414. Pharmacia Applied Health Outcomes Research Award: Development and validation of a pediatric nausea assessment tool for use by children receiving antineoplastic agents: preliminary analysis. *L. Lee Dupuis, M.Sc.Pharm., FCSHP*, Linda MacKeigan, B.Sc.Pharm., Ph.D., Anna Taddio, B.Sc.Pharm., M.Sc.Pharm., Ph.D., Elizabeth Kerr, Ph.D., Andrea Kelly, B.Sc.Pharm.; Hospital for Sick Children; University of Toronto, Toronto, ON, Canada.

The study purpose was to develop and validate an instrument to assess nausea intensity in children 4 to 18 years receiving chemotherapy.
A four-faced scale with a standard script for administration (pediatric nausea assessment tool [PeNAT]) was developed. Revisions were made following face validity testing with four pediatric oncology clinicians and four parents and pilot testing with 15 chemotherapy inpatients. Construct validity was evaluated by comparing PeNAT scores in 17 patients in each of 3 extreme groups: cancer chemotherapy recipients, cancer without chemotherapy, and no cancer. PeNAT scores were obtained 4 to 24 hours after chemotherapy; dietary intake (4-point scale) and emetic episodes were recorded for 4 hours prior. Criterion-related validity was evaluated by correlating PeNAT scores with emetic episodes and dietary intake in 36 chemotherapy recipients.
Mean PeNAT scores were low in all groups: 1.24, 1.18, and 1.24, respectively ($p>0.05$). PeNAT scores correlated significantly with emetic episodes (Spearman's rho = 0.52, $p<0.001$) but not with dietary intake. Only 1 of 14 children ≤ 8 years reported any nausea compared to 9 of 22 children > 8 years. Also, no emetic episodes were reported in children ≤ 8 years. Dietary intake correlated positively with nausea in children > 8 years (rho = 0.32) but negatively in children ≤ 8 years (rho = -0.31).
No differences in PeNAT scores were observed among children who were expected to have variable nausea intensity. A more extreme group, children undergoing bone marrow transplant conditioning, will be tested. Criterion-related validity was supported for emesis only. Children ≤ 8 years may experience less chemotherapy-induced nausea and emesis than older children and have a different dietary response. Further investigation of these potential effects of age is required.

415. Merck Cardiovascular Research Fellowship: Effect of β-adrenergic receptor polymorphisms on the response to metoprolol CR/XL in heart failure. *Steven G. Terra, Pharm.D.*, Karen K. Hamilton, M.D., J. Herbert Patterson, Pharm.D., Kirkwood F. Adams, M.D., Richard S. Schofield, M.D., Juan M. Aranda, M.D., James A. Hill, M.D., M.S., Daniel F. Pauly, M.D., Ph.D., Julie A. Johnson, Pharm.D.; University of Florida, Gainesville, FL; University of North Carolina, Chapel Hill, NC.

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