



# PSYCHOPHARMACOLOGY NEWSLETTER

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## THE IMPACT OF ATYPICAL ANTIPSYCHOTICS

*Douglas DelPaggio, PharmD., MPA, Director of Pharmacy Services, Alameda County Behavioral Health Care Services*

Recent literature indicates that the use of the newer antipsychotics may result in reductions in overall health care expenditures, increases in ambulatory services and improved clients' health care outcomes. Both Viale et al. and Carter et al. measured inpatient and outpatient costs, as well as medication costs, both before and after risperidone initiation. Using a comparable mean, the studies both documented a reduction of inpatient services and a shift towards lower costing outpatient care after initiation. Viale documented a monthly net cost increase of \$31 after risperidone initiation, whereas Carter's study group had an overall monthly cost saving of \$61. Blieden et al. examined the effects of clozapine treatment in a state hospital facility on costs, health status of clients, and discharge rate. For the clients who continued on clozapine for 6 months, there was a monthly savings of \$1,911 per client, and improvements on outcome measures such as the BPRS, the Negative Symptom Assessment, Hamilton D, and Quality of Life Scales. In addition, the discharge rate from the facility was higher for the clozapine group, as compared to those who discontinued the medication.

Unfortunately, these newer agents are costly. The average olanzapine prescription cost for Alameda County BHCS is \$310, as opposed to haloperidol at \$4. These four newer agents will cost ~\$350,000 in 1998, nearly 50% of our total medication budget. To document improved efficacy and evaluate costs for our Alameda County clients, the Office of the Medical Director initiated a prospective study in November of 1996 to study client symptom change, service utilization and health care expenditures in patients started

on atypical antipsychotics.

The BHCS study used the mirror image design to contrast costs and efficacy before and after initiation of the newer antipsychotics. The six-month period pre-index (prior to the start of the newer antipsychotic) and six-month period post-index (after the initiation) were studied using the pharmacy system data for pharmacy costs, and Insyst data system to track service cost. In addition, each client's psychiatrist prior to medication initiation and quarterly thereafter scored two symptom outcome measures, the Positive and Negative Syndrome Scale (PANSS) and the Abnormal Involuntary Movement Scale (AIMS).

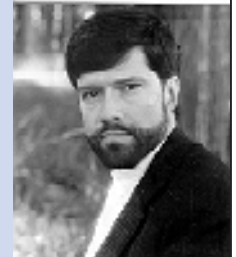
The PANSS consists of three sub-scales to measure the severity of schizophrenia: the Positive Symptom, Negative Symptom and General Psychopathology scales. Both the total Negative Symptom scale scores were used to measure antipsychotic efficacy during the post-index period. The AIMS measures symptoms of tardive dyskinesia, a debilitating movement disorder caused by conventional antipsychotics. Each client had their movements assessed by their psychiatrist using this scale throughout the post-index period.

Due to limited prescribing of the other new agents, only risperidone and olanzapine were included in this study. Because all MediCal clients' prescriptions are processed by the state, only non-MediCal clients receiving these agents through the BHCS Pharmacy System were enrolled with prescription information available through our Pharmacy System. The main questions posed were: would these agents 1) improve symptoms, 2) reduce high cost services, and 3) reduce overall expenses even though they cost



**Douglas DelPaggio, PharmD., MPA, Director of Pharmacy Services**

## From the Editor...



*As we enter our second year of publishing Bay Area Psychopharmacology Newsletter I would like to express my appreciation for the hard work of the editorial board which has lead to the successful launch of a regional update on psychopharmacology for community psychiatrists. I am particularly grateful to Sue Contreras for all her hard-work editing and doing the layout on the newsletter.*

*This edition we introduce a new regular feature: "Drug Information Consultation". If you have a specific psychopharmacology question you can now get a thoroughly researched answer from a team of clinical pharmacists and psychiatrists. The staff for this feature have access to several databases, including material that is not available from Medline. Each quarter the most interesting question or questions will be published in the newsletter.*

*Finally, I would like to encourage you to send me your comments or questions about the newsletter, at forster@itsa.ucsf.edu".*

**Peter Forster, MD  
Medical Director, Community  
Mental Health Services, San Francisco County**

more than older, cheaper medications? The following data pertains to the 28 clients in the risperidone arm of the study, and 46 olanzapine clients.

Although both risperidone and olanzapine were more expensive in the post-index phase as medications (Table #1), when all services were included, risperidone was associated with a slight cost increase of ~\$275 monthly per client. Olanzapine was associated with a reduction of overall costs by ~\$300 monthly per client.

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The olanzapine clients had a higher pre-index cost of all services due to a greater rate of client hospitalization (3.5 days per client) as opposed to risperidone (< 1 day per client). This difference may be attributed to the transition to treatment teams and the BHCS focus on high utilizing clients which coincided with FDA approval of olanzapine in late 1996.

Although risperidone clients had a slight increase in inpatient hospitalization days in the post-index period, (Table #2) there was a tendency to use less acute outpatient services such as outpatient visits, day

treatment, vocational training and medication visits. Most striking are the dramatic increases in outpatient services, vocational training and medication visits, which increased significantly in the post-index period.

With olanzapine initiation, there was a large drop in inpatient hospitalizations by 74%, (Table #3) correlating with a significant cost reduction per client, as well as a decrease in crisis visits. The data also showed increased utilization of outpatient services and client stabilization with an increase in outpatient services. Both agents demonstrated higher use of lower costing, ambulatory services in our system, and an increase in visits to higher functioning training programs.

Both atypical antipsychotics had a major impact on the symptoms of schizophrenia. Almost 85% of the clients in each arm of the study had scale scoring (PANSS, Negative Subscale, AIMS) completed by their respective psychiatrist. Listed in the table are the mean scores both prior to and post initiation of each antipsychotic.

Table 1 **COST PER CLIENT PER MONTH**

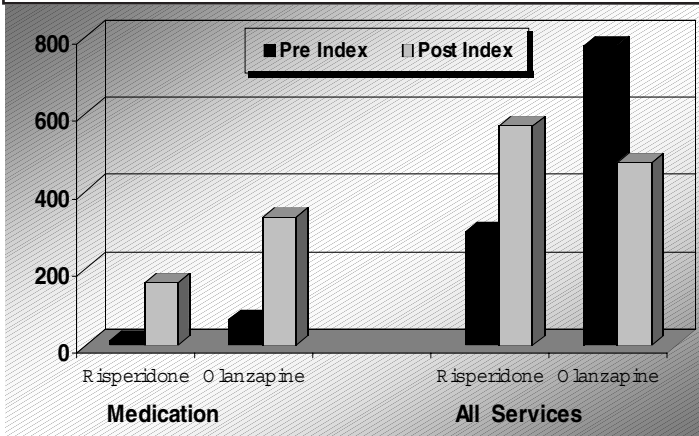


Table 2 **RISPERIDONE: # VISITS vs SERVICES**

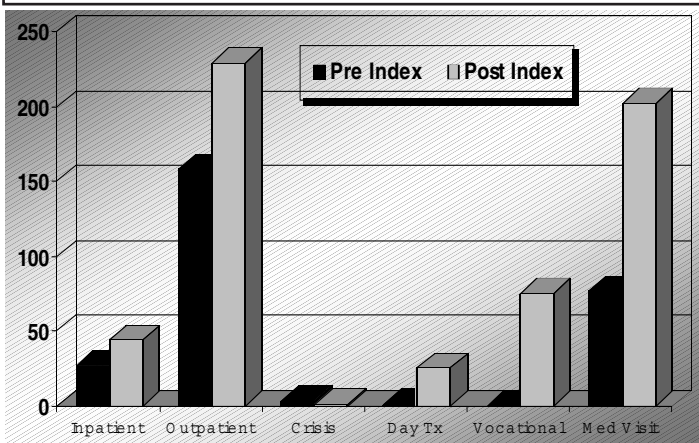
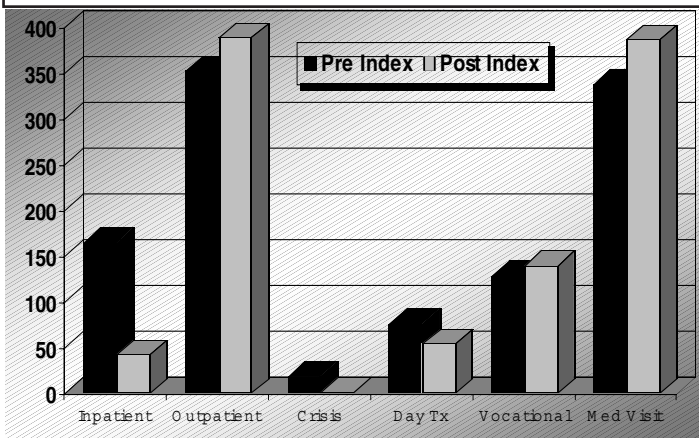


Table 3 **OLANZAPINE: # VISITS vs SERVICES**

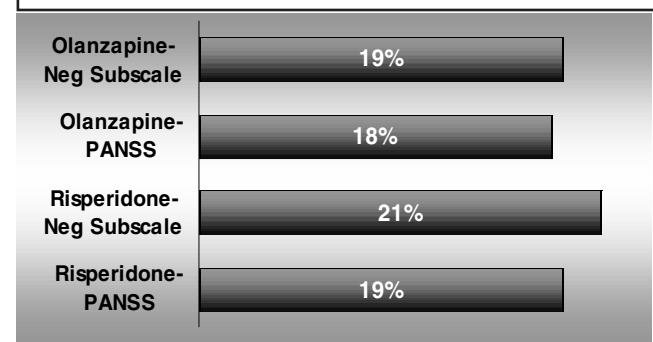


Risperidone Mean	PANSS	Neg Subscale	AIMS
Prior to Initiation	86.09	24.57	6.57
After Initiation	69.74	19.43	5.86
Olanzapine Mean	PANSS	Neg Subscale	AIMS
Prior to Initiation	80.77	22.18	9.21
After Initiation	65.92	17.87	2.64

As measured by the PANSS, there was an average decrease (improvement) in scores of almost 20% (Table #4) with both agents. This documents improvement in client symptoms with both of these agents. In addition, the symptoms measured by the negative subscale were also decreased by an average of about 20%. The impact on these formerly treatment resistant symptoms is a major benefit of the newer antipsychotics compared with conventional agents. Although few clients had symptoms of tardive dyskinesia, both agents showed an average reduction in the AIMS scores, pointing to symptom reduction.

In conclusion, our study supports the use of the higher costing newer antipsychotics due to their impact on resistant symptoms, client services, and overall costs. Both agents reduced symptoms of schizophrenia, and associated negative symptoms. Currently, olanzapine demonstrates an overall cost savings of ~\$300 monthly, and risperidone, a cost increase of \$275 monthly. The reduction of costly services and client stabilization offset the price of these medications. Risperidone's cost increase may be due to the smaller sample size in the group, and lower pre-index cost for these clients. The study will be continued over the next 12 months for additional clients and data.

Table 4 **% REDUCTION PANSS/NEG SUBSCALE PRE-INDEX AND POST-INDEX**



# ALAMEDA COUNTY BEHAVIORAL HEALTH CARE

## BHCS MIA MEDICATION PROGRAM

Richard P. Singer, MD, Medical Director

Douglas DelPaggio, PharmD., MPA, Director of Pharmacy Services

Implemented in February 1998, the BHCS MIA Medication Program coordinates the drug companies indigent medication (MIA) programs with our clients, clinics and pharmacy network. There are two components to our MIA Program. For the short term, medication vouchers offer a 7-30 day supply of drug, whereas bulk medications offer a renewable 3-month supply of drug. Initially, medication vouchers are used with our non-insured clients, until the application is processed by the drug company, and bulk medications are shipped.

On a county wide basis, this program has deferred the costs of prescribing expensive newer medications for non-insured clients to the drug companies' indigent patient programs. The application process is both time and labor intensive, requiring complete financial information, documentation, and signatures. In addition, each drug company has a different program to provide medication to the indigent population. We are currently coordinating five different MIA programs and, as of December 1998, have processed over 125 MIA applications.

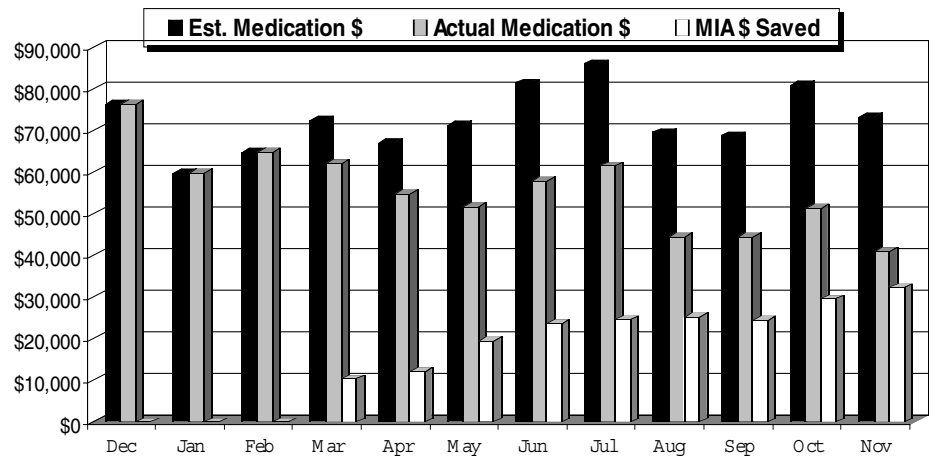
Each BHCS Mental Health Program has a corresponding network MIA Pharmacy in which to directly work. Our BHCS Psychiatrists must attach a medication voucher to each client prescription, until the bulk medication application is completed, and the drug is shipped. United Parcel Service (UPS) plays an integral role in both delivering the bulk medication from the drug company to the program, and then from the program to the assigned MIA Pharmacy. In addition, UPS will deliver the labeled medication to the client after pharmacy dispensing. The BHCS MIA Medication Program is coordinated through our pharmacy system, run by our Director of Pharmacy Services.

The medications included in this program are the top costing psychoactive medications for BHCS: the newer antipsychotics (Zyprexa, Risperdal, Clozaril) and antidepressants (Prozac, Paxil). In 1997, these five agents

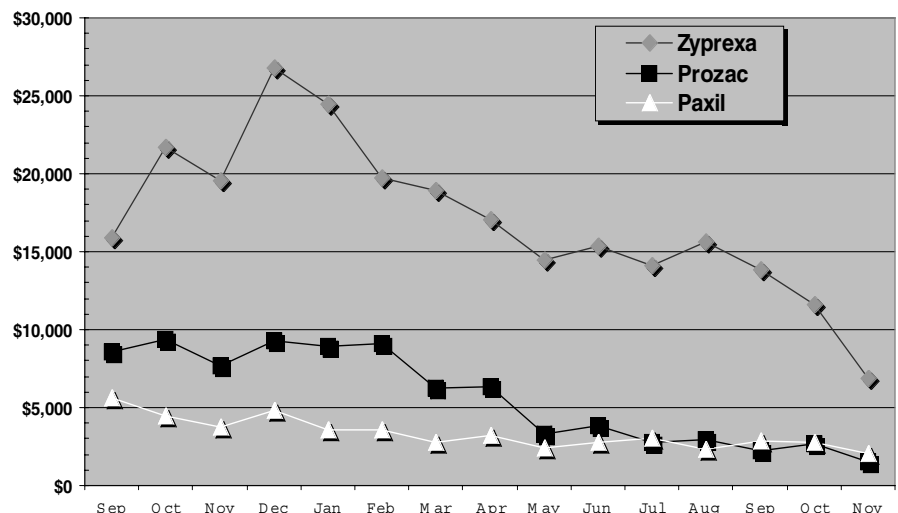
accounted for almost 65% of the total medication budget, approximately \$460,000. For 1998, we have deferred over \$225,000 to the drug manufacturers through the BHCS MIA Program, at an average rate of \$25,000 monthly ( Budgeted Cost Comparison Chart). The dollars spent on antipsychotic Zyprexa

have dramatically decreased from a monthly high of \$27,000 to \$7,500 a decrease of over 70% (Medication Cost Comparison Chart). Furthermore, the monthly medication costs for both Paxil and Prozac have dropped almost 75% through this program.

### BUDGETED COST COMPARISON 1997-1998

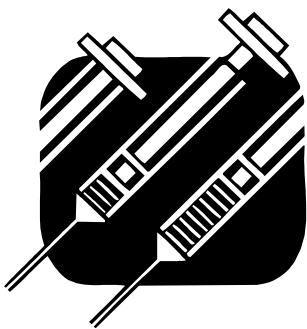


### MEDICATION COST COMPARISON 1997-1998



## BODY FLUIDS IN ACTION

Working with the Psychiatric Practices Committee since October 1995, this Office has established various guidelines, protocols and standards related to our medical practice in Behavioral Health Care Services. Just when you think you've pretty much covered it all, something else invariably pops up (no pun intended), this time involving the management of needle sticks and other body fluid exposures.



The Alameda County Medical Center does have a procedure for responding to the accidental exposure to blood and other body fluids which has been available to BHCS outpatient sites as well. We are in the process of modifying it, however, for more specific application to our own structure. In addition, as we have introduced on site testing for alcohol and other drugs, we now need guidelines for the appropriate handling of specimens and specimen containers at our Community Support Centers. Development of this is occurring and after review by Human Resources, the guidelines and procedures for all of the above will be distributed.



## BHCS PHARMACY SYSTEM: EFFICIENCY, EFFECTIVENESS AND COST AVOIDANCE

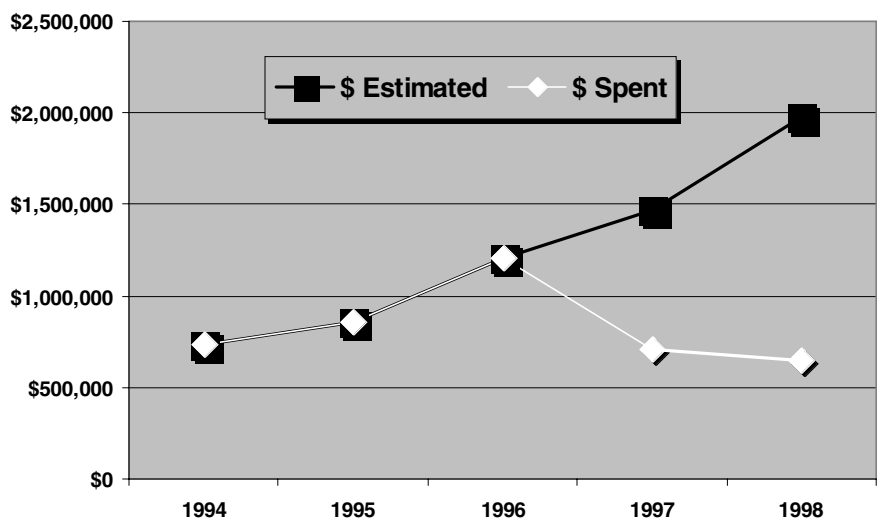
Prior to the implementation of the BHCS Pharmacy System, medication costs were rapidly escalating at an average rate of 130% times of the previous year's costs. BHCS medications costs rose to over \$1.2 million in 1996 (see chart below). Furthermore, Zyprexa, the newest, most expensive antipsychotic agent was approved by the FDA in October 1996, and forecasted to increase drug costs by an additional 30-50%. To reduce these expenditures, and to facilitate medication services, a Pharmacy Benefit Management (PBM) company was contracted in late 1996, coordinated by our BHCS Pharmacy Director. Other challenges included increasing client access to medications, number of network pharmacies, and programs covered.

Over the past two years, the BHCS Pharmacy System has effectively addressed these challenges, as well as resulted in a large cost avoidance. This system provides access to psychiatric medication and pharmacy services for the chronically mentally ill people of Alameda County that are indigent. From the limited coverage previously offered, the Pharmacy System has expanded medication services to all 18 mental health clinics and to all 16,000 clients receiving services through BHCS. To improve pharmacy access and support medication compliance, an expanded network of 46 strategically located pharmacies, medication delivery, language specialty sites and extended hours were implemented.

Delivery services have been arranged to transport medications from the pharmacy to the client's home, living shelter or clinic where services are coordinated. In an effort improve the quality care to all clients, medication dosing ranges, a medication formulary system, and medication Practice Standards of Care were established. By designing and maintaining a Medication and Pharmacy User Guide, the dissemination of information is facilitated to all practitioners.

Financially, the pharmacy system has provided uniform reimbursement and correct payer source billing. By correcting the billing alone, the pharmacy budget has reflected a cost avoidance of over \$500,000 in just the first year of the program. In addition, through the BHCS MIA Medication Program, over \$225,000 additional dollars have been saved. Overall, since the system's inception, almost \$2,100,000 has been avoided (Table #1). Results of these savings include treating more clients, open access for the use of newer, higher costing medications, and continuing open services for the chronically mentally ill in Alameda County with limited funds.

## BHCS MEDICATION COSTS



# BAY AREA PSYCHO- PHARMACOLOGY LAUNCHES MENTAL HEALTH DRUG INFORMATION COLUMN

The Bay Area Psychopharmacology Newsletter is now offering clinicians a forum to ask drug information questions regarding mental health drug therapy and related problems. Questions can be mailed to the newsletter and selected questions and responses will be published quarterly as space allows. Clinicians who submit questions will also receive a personal response to each question that they submit. It is hoped that the quarterly column will serve as a valuable forum for the dissemination of drug information that is of use to many readers.

Psychopharmacology questions might include:

- dosing and designing drug regimens
- evaluation of drug interactions
- assessment of adverse drug effects
- information on drug stability
- drug use in pregnancy and lactation
- practice guidelines and treatment algorithms

Drug information consultations will be based on primary literature evaluation when required. Research and literature analysis will be performed by a clinical pharmacist with consultation from a community psychiatrist.

Please submit questions to the address below. If you would like a personal response, please be sure to include your name and contact information.

Bay Area Psychopharmacology  
Newsletter  
2532 Santa Clara Avenue, Suite 219  
Alameda, CA 94501

## CLINICAL TRIALS



Barbara Liang, Pharm.D

### Bupropion for Depression

52 week, multicenter, randomized, double-blinded, placebo-controlled study evaluating relapse and recurrence of depressive symptoms after 8 weeks of open label dosing. Investigator: Alan J. Cohen, M.D., Berkeley/Walnut Creek. (510) 649-8444.

### Depakote in Children of Bipolar Parents

A 12 week open label study for children 6-18 with a mood or behavioral disorder. Children must have at least one biological parent with Bipolar I or II disorder. Investigator: Kiki Chang, MD, (650) 725-0956; Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine.

### DHEA Effects on Mood, Memory, and Well Being in Healthy Males

Study to investigate the cognitive affective and personality effects of DHEA in psychiatrically and medically healthy men between the ages of 56-85. Investigator: Louann Brizendine, MD, (415) 476-7840, ext.2, UCSF Department of Medicine.

### Ginkgo Combination Formula for treatment of Sexual Dysfunction secondary to antidepressant therapy

Double-blinded, placebo-controlled study to evaluate the safety and efficacy of a new Ginkgo combination formula in patients

experiencing sexual dysfunction related to antidepressant therapy. Investigator: Alan J. Cohen, MD, Berkeley/Walnut Creek. (510)649-8444

### Olanzapine vs Haloperidol in First Break Psychosis

Double-blind, 2 years study of olanzapine vs haloperidol in schizophrenic or schizoaffective patients experiencing a first psychotic break. Investigator: Ira Glick, MD, (650) 723-6678; Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine.

### Olanzapine "Rescue" Study

A 10 week open add-on of olanzapine in acute exacerbations of bipolar depression, mania, hypomania or mixed episodes. Open to patients with Bipolar, Bipolar II or Bipolar NOS disorders on any or no medications. Investigator: Terrence Ketter, MD, (650) 498-4968; Dept. of Psychiatry and Behavioral Sciences, Stanford University School of Medicine.

### Topiramate in Acute Mania

A 3 week, double-blind, placebo-controlled study for Bipolar I patients experiencing manic symptoms. Investigator: Terrence Ketter, MD, (650) 498-4968; Dept of Psychiatry and Behavioral Sciences, Stanford University School of Medicine.



## DRUG INFORMATION CONSULTATION

Is there a drug-drug interaction between lithium and gabapentin?

Edited by Renee Williard, Ph.D.

**Both lithium and gabapentin are eliminated by renal excretion exclusively. Theoretically, a competitive drug-drug interaction could alter lithium excretion and be of clinical significance given lithium's narrow therapeutic window. A recently published placebo-controlled study (Frye M, Journal of Clinical Psychopharmacology, 1998; 18(6):461-464) examined the effects of gabapentin on single dose (600 mg) lithium pharmacokinetics in thirteen patients. Data indicated that gabapentin does not cause clinically significant changes in single-dose lithium pharmacokinetics in patients with normal renal function. Although additional controlled multiple-dose studies in larger, more heterogenous samples are needed, the study suggests that gabapentin and lithium may be administered in combination in the treatment of bipolar disorder.**



# CONTINUING MEDICAL EDUCATION

Douglas DelPaggio, PharmD., MPA, Director of Pharmacy Services

## March, 1999

<b>3/9/99</b>	<b>Forbidden Fruit: Perspectives in Adolescent Sexuality, Lynn Ponton, M.D.</b>
12:15 - 1:45 p.m.	San Mateo County Mental Health Services, 225 W. 37th Ave., Multi-Purpose Room, San Mateo (650) 573-2530
<b>3/16/99</b>	<b>Seeking an Analytic Identity, Alan Skolnikoff, M.D.</b>
12:15 - 1:45 p.m.	Mills Peninsula Health Services, 1783 El Camino Real, Sierra Rooms, Burlingame (650) 696-5313
<b>3/23/99</b>	<b>Agitation and Paranoia in the Demented Elderly, Robert B. Portney, M.D.</b>
12:15 - 1:45 p.m.	San Mateo County Mental Health Services, 225 W. 37th Ave., Multi-Purpose Room, San Mateo (650) 573-2530
<b>3/24/99</b>	<b>Motivating Patients with Negative Symptoms, John Strauss, M.D., Yale University School of Medicine</b> <i>Alan S. Bellack, Ph.D., University of Maryland School of Medicine</i>
10:00 - 11:30 a.m.	Teleconference: Ala. Co Behavioral Health Care Srvs., 2000 Embarcadero Cove, Ste. 400 Alameda Rm., Oakland (510) 567-8106
<b>3/26/99</b>	<b>Dementia and Psychosis, Prakash Masand, M.D., SUNY Health Science Center</b>
11:45 a.m. - 1 p.m.	San Francisco General Hospital, 1001 Potrero Ave., Room 7M30 San Francisco (415) 206-4938

## April, 1999

<b>4/6/99</b>	<b>The Mentally Ill Behind Bars, Terry Kupers, M.D.</b>
12:15 - 1:45 p.m.	Mills Peninsula Health Services, 1783 El Camino Real, Sierra Rooms, Burlingame (650) 696-5313
<b>4/20/99</b>	<b>Life in Russia, Theodore Myers, M.D.</b>
12:15 - 1:45 p.m.	Mills Peninsula Health Services, 1783 El Camino Real, Sierra Rooms, Burlingame (650) 696-5313
<b>4/28/99</b>	<b>Innovations in Cognitive-Behavioral Therapy: What It Can &amp; Cannot Do for the Seriously Mentally Ill, Jeffrey Young, Ph.D., Columbia University</b>
10:00 - 11:30 a.m.	Teleconference: Ala. Co Behavioral Health Care Srvs., 2000 Embarcadero Cove, Ste. 400 Alameda Rm., Oakland (510) 567-8106
<b>4/30/99</b>	<b>Antipsychotics: Past and Future Endeavors, Samuel Keith, M.D.</b>
11:45 a.m. - 1 p.m.	San Francisco General Hospital, 1001 Potrero Ave., Room 7M30, San Francisco (415) 206-4938

## May, 1999

<b>5/4/99</b>	<b>Spoiling Childhood: The Crisis for American Parents and Their Children, Diane Ehrensaft, Ph.D.</b>
12:15 - 1:45 p.m.	Mills Peninsula Health Services, 1783 El Camino Real, Sierra Rooms, Burlingame (650) 696-5313

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