Bay Area

PSYCHOPHARMACOLOGY NEWSLETTER

Volume 2, Issue 2 **June, 1999**

GRAND ROUNDS IN COMMUNITY MENTAL HEALTH

PHARMACOTHERAPY OF PSYCHIATRIC DISORDERS IN PATIENTS WITH COMORBID DRUG AND ALCOHOL ABUSE

This article is adapted from a ground rounds presentation by ***Steven L. Batki, MD,***
Clinical Professor, UCSF Dept of Psychiatry;
Director, SFGH Division of Substance Abuse and Addiction Medicine

The Significance of Comorbidity

Substance abuse and psychiatric disorders coexist in a large number of patients, particularly among those seen by public and community mental health systems. Comorbidity is common. For example, the Epidemiologic Catchment Area (ECA) report indicated that 47% of patients with schizophrenia had some form of substance abuse. In fact, schizophrenics had the second highest rate of substance abuse among all psychiatric disorders in the ECA study, with the exception of borderline personality disorder. Among schizophrenics, the prevalence of alcohol abuse was nearly 34% and the prevalence of other drug abuse was nearly 28%. In schizophrenics, studies have shown that the presence of drug and alcohol abuse leads to greater use of psychiatric services, more frequent incarcerations, earlier onset of illness, more positive symptoms, and more disorganization and depression.

Abuse Potential of Psychiatric Medications

The only medications that we need to worry about, with respect to abuse potential, are the benzodiazepines and other CNS depressants, and the psychostimulants, such as methamphetamine and methylphenidate (Ritalin). Generally, all other psychiatric medications, including antidepressants, antipsychotics, mood stabilizers, non-benzodiazepine anti-anxiety medications, and anti-Parkinsonian medications are not abusable to any significant degree. Occasionally, we do encounter patients who will overuse or misuse anti-Parkinsonian medications or sedating tricyclic anti-depressants, but these are the rare exception rather than the rule (See Table, below).

Abuse Potential of Psychiatric Medications

NO POTENTIAL	LITTLE, IF ANY	ABUSEABLE
antipsychotics	tricyclic anti-depressants	benzo-diazepines
lithium	anti-Parkinsonians	other CNS depressants
buspirone	anti-convulsants	metham-phetamine
new anti-depressants		methyl-phenidate

Diagnosis of Substance Use Disorders

Diagnosing substance abuse among patients with psychiatric disorder depends on the same assessments that we use for any other medical or psychiatric problem: history, examination, and laboratory testing. Of these, careful history is the most important. It is helpful to talk to previous caretakers, to look at the medical record, and to ask family members, as patients may seek to minimize or deny their drug and alcohol use. A mental status examination may reveal symptoms that are specific to drug intoxication, for instance hallucinations in unusual modalities (visual or tactile). The physical examination may reveal skin signs of drug use, such as injection marks ("tracks" or old injection scars). Urine drug testing may reveal the use of drugs of abuse, generally for up to 72 hours for most drugs. Breath alcohol testing is useful in individuals who are alcoholic, and blood tests, particularly those that check for liver enzymes such as the transaminases, can show elevations that are associated with alcohol use. Another useful measure is the mean cell volume (MCV) which may be elevated (greater than 100) in the presence of active alcohol use.

Pharmacotherapies for Substance Abuse

What kinds of medical treatments and medications can we use for substance use disorder? In general, the types of medications used for drug abuse involve either 1. replacement or substitution using agonists, 2. the use of antagonists, 3. the use of aversive medications, or 4. medications that seek to correct some underlying psychiatric pathology. Examples of medications that replace drugs are agonists such as methadone for opiates, nicotine for smoking, or benzodiazepines for alcohol withdrawal. An example of antagonism is the use of naltrexone (Revia) for opiate or alco-

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THE USE OF NEW THIRD GENERATION AEDS IN BIPOLAR DISORDER

Renée Williard, RPh, PhD
Peter Forster, MD

Newer third generation anti-eleptic drugs (AEDs) have recently begun to be used by psychiatrists alongside the established second generation AEDs: carbamazepine (Tegretol) and valproate (Depakote). A summary of the use of gabapentin (Neurontin), lamotrigine (Lamactil), and topiramate (Topamax) in bipolar spectrum disorders is presented in the table on page 2.

The effectiveness of gabapentin, lamotrigine, and topiramate in bipolar disorders is currently under study. The literature consists primarily of a limited number of preliminary abstracts, letters to the editor, and small studies of varying quality. All of the reported studies (with the exception of a recent lamotrigine study) have design limitations including open, uncontrolled, or retrospective data; small study sizes; and the confounding use of concomitant medications. Further prospective controlled data are required to clearly establish the effectiveness of these agents as monotherapy or adjunctive therapy in the various subgroups of patients with bipolar disorder.

INSIDE THIS ISSUE

Summary of the Use of Third Generation AEDs in Bipolar Disorder

	Gabapentin	Lamotrigine	Topiramate
Pharmacology	Increases GABA levels. Structurally related to gamma-aminobutyric acid (GABA).	Blocks sodium channels and inhibits release of glutamate.	Blocks sodium channels, enhances GABA receptors, and blocks glutamate.
Pharmacokinetics	T1/2 = 5-6 hours	T1/2 = 24 hours Linear pharmacokinetics in doses up to 700 mg.	T1/2 = 20-36 hours Linear pharmacokinetics in doses up to 800 mg.
Route of Elimination	Renal	Hepatic	Primarily renal
Dosage Range	200-3600 mg/day in three divided doses. Generally start with 100mg TID increasing to 200 - 300mg TID.	Initial dose of 12.5-50 mg/day (QD) titrated to a final dose 50-500 mg/day in two divided doses. Titrate by gradually adding 12.5-50mg each week for 8 weeks. Slower titration recommended if patient is on valproate.	Initial dose of 25 mg QD or BID titrated to a final dose between 100 and 200 mg/day, rarely up to 400 mg/day in two divided doses. Titrate by adding 25-50 mg each week for 8 weeks.
Common Side Effects	Somnolence . . . . . .24% Dizziness . . . . . .20% Ataxia . . . . . .17% Fatigue . . . . . .15% Headache . . . . . .15% Tremor 15%	Ataxia . . . . . .17-28% Dizziness . . . . . .17-54% Nausea . . . . . .17-25% Headache . . . . . .15-32% Vomiting . . . . . .15-18% Rash 10-15%	Somnolence . . . . . 30% Dizziness . . . . . 28% Vision problems . . . . . 28% Psychomotor slowing . . . . . 17% Nervousness 16%
Drug Interactions	- Minimal to none (No interaction found with lithium in a single-dose study).	- Carbamazepine may induce metabolism of lamotrigine (reports are inconsistent) and lamotrigine may increase carbamazepine toxicity - Lamotrigine may reduce plasma levels of valproate and valproate may increase lamotrigine concentrations	- Carbamazepine and valproate may lower plasma levels of topiramate by 50% and 15% respectively. - Topiramate may reduce plasma levels of valproate by 10%. - No interactions reported with lithium, gabapentin, or lamotrigine - May lead to decreased effectiveness of some oral contraceptives
Lab Monitoring	None	None	None
Precautions	Dose reduction required in renal impairment	Associated with severe life-threatening rashes*. Lamotrigine should be discontinued at the first sign of rash.	Dose reduction required in renal impairment
Advantages/ Indications	- Quite effective for anxiety and pain symptoms - Relatively benign side effect profile - Perhaps most effective for rapid cycling?	- Definitely effective for bipolar depression - Appears to also reduce manic recurrences	- In some patients may cause significant weight loss which can be useful when adding to other agents that cause weight gain - May be effective in rapid-cycling and mixed bipolar states not controlled by carbamazepine or valproate
Disadvantages/ Contraindications	- In controlled studies, less effective than lamotrigine in bipolar depression - Dose-dependent bioavailability of 60% for doses of 600 mg or less. Bioavailability decreases substantially for doses > 600 mg.	- Very slow titration needed - Causes rash and rare Stevens Johnson Syndrome*	- Least data on effectiveness; some patients appear to get worse - Some patients are very sensitive to CNS side effects
Cost (per tablet)	100 mg . . . . . $0.36 300 mg . . . . . $0.91 400 mg $1.09	5 mg . . . . . .$1.46 25 mg . . . . . $1.54 100 mg . . . . . $1.63 150 mg . . . . . .$1.72 200 mg $1.80	25 mg . . . . . $1.02 100 mg . . . . . .$2.33 200 mg $2.72
Cost (per month)	1800 mg/day $163.80	300 mg/day $103.20	200 mg/day . . . . . $139.80 200 mg/day (split 200 mg tablet) $81.60
Formulary Status**	Alameda . . . . . .NF, PAR San Francisco . . . . . .NF, PAR San Mateo . . . . . .F Santa Clara . . . . . .NF, PAR	Alameda . . . . . .NF, PAR San Francisco . . . . . .NF, PAR San Mateo . . . . . .NF, PAR Santa Clara . . . . . .NF, PAR	Alameda . . . . . .NF, PAR San Francisco . . . . . .NF, NA San Mateo . . . . . .NF, PAR Santa Clara . . . . . .NF, NA

***** The incidence of life-threatening rash with lamotrigine (including Stevens-Johnson syndrome and toxic epidermal necrolyis) is 1/1000 in adult patients and 1/50 in pediatric patients. There are suggestions yet to be proven that the risk of rash may be increased by 1) coadministration of lamotrigine with valproate, 2) exceeding the recommended initial dose of lamotrigine, or 3) exceeding the recommended dose escalation of lamotrigine.

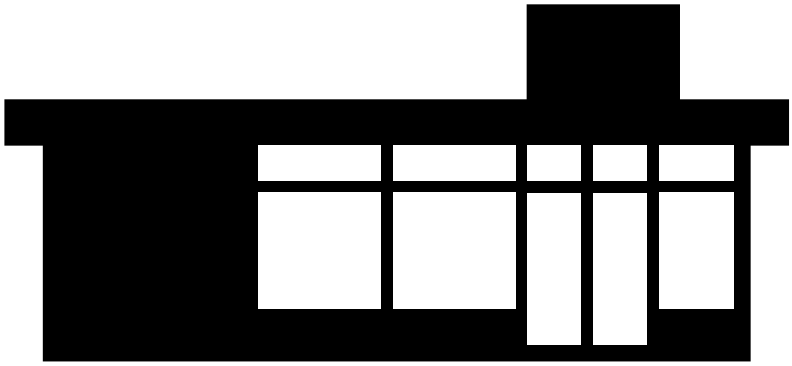
****** **NF**=nonformulary, **PAR**=prior authorization request, **NA**=not available, **F**=formulary

ALAMEDA COUNTY
BEHAVIORAL HEALTH CARE

NEW PRIMARY CARE MEDICAL CLINIC OPENING

Richard Singer, M.D.

Behavioral Health Care Services, working with Dave Kears, Director of the Health Care Services Agency, is pleased to announce the opening on March 15, 1999 of a new primary care medical clinic designed to accommodate people with mental health problems. Located at 10520 MacArthur Boulevard in Oakland one block from the San Leandro city limits, it is an extension of the already existing medical practice of Uchenna A. Okoronkwo, II, M.D. and Ralph L. Peterson, M.D..



10520 MacArthur Boulevard
Oakland, California

Referrals are being accepted for all adult and child patients, with or without insurance, who may require the medical services of a primary care physician. Working with the clinic staff is a nurse with psychiatric experience, assisting in the provision of both physical health care and primary care-based mental health treatments to patients referred by BHCS mental health programs. Such referrals include the following:

1. Any mental health patient in need of physical health care who does not already have a primary care physician
2. Any mental health patient whose psychiatric symptoms may be caused by a physical medical problem, including organic brain syndrome and mental retardation
3. Adult mental health patients in need of ongoing psychotropic medication maintenance; must be stabilized on psychiatric medication for at least one year with no hospitalizations or Psychiatric Emergency Room visits during that time.
4. Adult patients assessed at ACCESS and determined to have no current need for specialty psychiatric services but whose mild to moderate anxiety or depression could benefit from primary care physician evaluation and treatment.
5. Patients needing physical health care and determined to have behaviors too difficult for most primary care clinics to manage; referral may come from ACCESS as well as any BHCS or primary care clinic
6. Child and adolescent patients who do not already have a primary care physician:
   a) those with uncomplicated ADHD in need of initial treatment, i.e., without concomitant conditions such as depression, anxiety, aggressiveness
   b) those with ADHD already being prescribed medication, e.g. from out-of-county; these may either be treated or referred back to ACCESS
   c) those with ADHD treated by a psychiatrist and stable on medication for at least 6 months; they may or may not continue to have a Level I or III therapist while being medicated by a primary care physician
   d) those with a mood disorder and stable on medications for at least 9 months

Completion of a standard referral form provided by the Primary Care Medicine Clinic is required for all referrals to the clinic. The referral process includes:

a. Call for appointment at (510) 569-7326
b. Identify that you are from ACCESS or a BHCS program
c. Complete referral form and either fax to clinic (510) 635-9025, mail it or have it hand carried so it is available when patient is seen by the physician

Timely communication between physicians is an essential element of this primary care/mental health care interface. As with any other primary care physician, telephone consultation with an ACCESS psychiatrist will be made immediately available to the Primary Care Medicine Clinic physician requesting it, as follows:

a. Call (510) 346-1000 or 1-800-491-9099.
b. As soon as message starts, push "3" for adult issue,"2" for child issue
c. When the licensed mental health clinician answers, caller identifies self as a primary care physician wanting direct consultation with a psychiatrist. Caller will be put on a brief hold and the psychiatrist will

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BHCS FORMULARY ADDITIONS: NEWER ANTI-DEPRESSANTS

As of March 1st, the BHCS Psychiatric Practices Committee added two antidepressants to our medication Formulary. Both venlafaxine (Effexor) and mirtazapine (Remeron) work through blocking several neurotransmitters/receptors in the CNS to provide relief for depression. Venlafaxine blocks the reuptake of the neurotransmitters norepinephrine (NE) and serotonin (5-HT), while mirtazapine stimulates both NE and 5-HT release, through the blockade of the alpha autoreceptor. Both agents have been on the market for over 4 years, and have been prescribed by BHCS psychiatrists in previous responders or medication resistant cases of depression. Some common adverse effects with venlafaxine include dry mouth, insomnia, agitation and sexual dysfunction. Mirtazapine may cause sedation, weight gain and dry mouth. Although both agents are on the MediCal list, with venlafaxine only the extended release form (Effexor XR) is covered. In addition, both agents have a 9-month MediCal prescribing restriction. The average daily cost for the agents is as follows:

Mirtazapine	$2.20
Venlafaxine	$3.75

MOSBY'S GENRX ON-LINE

Another benefit of the expanding IS network is the availability of references on-line. Mosby's GenRx is available in an on-line format on our server. This complete resource of all brand and generic medications includes complete medication monographs, an excellent drug/food/lab interaction tool, and search mechanism. Currently, it is available in the BHCS Library, both Access sites, Fremont Family Resource Center (Tri-City) and Eden Community Support. As the network expands, more sites will have this useful resource, as well as others we are exploring.

MIA PROGRAM ADDITIONS

It has been over a year since the implementation of the successful BHCS MIA Program. With the co-operation of clients, staff, psychiatrists and network pharmacists, monthly medication costs have been cut by almost 40%, reflected in the continuing policy of open access to newer medications for all BHCS clients. The growing list of medications currently part of this program now includes:

- **Depakote**
- **Haldol Decanoate**
- **BusPar**
- **Serzone**
- **Seroquel**
- **Prozac**
- **Paxil**
- **Zyprexa**
- **Risperdal**
- **Clozaril**

NEW PRIMARY CARE MEDICAL CLINIC OPENING

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be immediately contacted, interrupting a session if necessary.

d. Non-medication, non-medical consultations (e.g. referral to ACCESS information, mental health resources) will be with an ACCESS licensed clinician.

BHCS psychiatrists whose stable patients have been referred to the Primary Care Medicine Clinic will continue to be available for consultation on those patients. In addition, periodic re-assessments by the psychiatrist may be requested by the primary care physician, as clinically indicated.

Finally, unsuccessful attempts to treat patients for their mental health needs in this or any other primary care setting will be referred back to the referring source for further psychiatric assessment and treatment and/or referral to a specialty mental health provider.

Depending on the volume and geographic distribution of referrals, expansion to other areas of the county will be considered as data is collected and analyzed. An oversight committee has been established to address problems as they occur. It meets monthly and any issues concerning services may be routed to either Drs. Okoronkwo and Peterson, or to the Medical Director's Office liaison to the project, Catherine Peterson, R.N. at (510) 567-8108.

For additional information concerning the referral process and to make referrals, the clinic may be contacted at (510) 569-7326.

This is an important first step in the development of primary care services within Alameda County for clients with mental illness and we look forward to expanding these services to those with substance abuse problems as well.

Santa Clara County
Mental Health Services

MENTAL HEALTH PHARMACY

BULLETIN

The December Pharmacy Bulletin 452 states that " a prescription will be denied if the duration of therapy is exceeded without a TAR".

- The duration of therapy is defined as "a period of time starting with the date of the first prescription and lasting for a fixed number of days from the start date". The time period is for consecutive days, not a cumulative period based on each prescription's "days supply".
- Presently, the duration of therapy for single drugs and drug groups are:

Single Drugs	Duration in Days
Clonazepam	90
Cisapride	90
Bupropion (Immediate release tabs only)	270
Fluoxetine	270
Fluvoxamine	270
Mirtazapine	270
Nefazodone	270
Paroxetine	270
Venlafaxine (Extended release capsules)	270

Drug Groups	Duration in Days
H2 Blockers	90
Proton Pump Inhibitors	90

- Duration of therapy applies even if different pharmacies supply the drug.
- Tars submitted for the above drugs "must establish a medical necessity for continuation of therapy. This information should include an updated status of the patient as well as maintenance doses and alternate therapies where appropriate".
- Zoloft is not on the Medi-Cal list of contract drugs so a TAR is required.
- Effective January 1, 1999 Effexor XR (37.5 mg, 75 mg, and 150 mg) was added to Medi-Cal list of contract drugs - Pharmacy Bulletin 453.

UPDATE

As of December 1, 1998, all Medi-Cal patients who have been receiving Klonopin (clonazepam) for 3 months or more and Wellbutrin (bupropion), Prozac (fluoxetine), Luvox (fluvoxamine), Remeron (mirtazapine), Serzone (nefazodone), and Paxil (paroxetine), for 9 months or more will require a TAR (Treatment Authorization Request) to continue to receive the above drugs.

As of January 1, 1999, Effexor-XR (venlafaxine) is on the Medi-Cal list of contract drugs with the same 9 month restriction that the above antidepressants have.

Also, Zoloft (sertraline) is not on the Medi-Cal list of contract drugs and does require a TAR for the patient to receive it.

SANTA CLARA VALLEY HEALTH & HOSPITAL SYSTEM

Psychiatric Medication Management Committee

Kurt Swensen, MD
Co-Chairperson Psychiatric Medication Management Committee
The committee meets every other Thursday in Central Mental Health

This unique skills group is an offshoot of a committee formed 10 years ago under the auspices of special funding from the Santa Clara County Board of Supervisors. At that time it was a group designed to monitor and approve the use of an amazing yet potentially lethal new medication: **Clozaril.**

The committee is composed of a small core group of members. It includes the Medical Director of the Department of Mental Health, two Pharm.D.'s, three lead psychiatrists, and a mental health care analyst and a LCSW specializing in long-term care. At times other visitors come for specialized needs such as child psychiatrist, contact-agency representatives, forensic psychiatrist and acute care psychiatrists . The committee reports to the Psychiatric Practices Committee of SCVS&HS which is the highest medical body chaired by Soleng Tom, MD, Department of Mental Health Medical Director. Dr. Tom also oversees the Medication Monitoring Committee and often meets with the committee.

The committee's duties have expanded tremendously over the years beginning with the release of Risperidone. It became important to consider cost-benefits outcomes with the ever spiraling pharmacy budget.

The first new endeavor of the committee was to participate in a published research study measuring outcomes of treatment with Risperidone entitled, "Impact of Risperidone on the Use of Mental Health Care Resources" *Psychiatric Services*, Sept 1997, Vol.48, No.9. Later the committee served to monitor the use of all novel neuroleptics, newer medications and new uses of older medications. The intent has always been to provide the highest quality of care in the most cost effective way. SCC has always considered itself duty bound to provide the best of care whether a patient is insured or indigent.

Our system of Care treats roughly 7,000 seriously mentally ill patients, including outpatient, inpatient, State hospital patients, patients in IMD's, and patients in the criminal justice system.

Over time the committee expanded its role in standardizing treatment interventions and outcomes. Currently the committee is charged with the following mission:

1- Developing standardized medication consent forms in multiple languages.
2- Modernizing medication treatment @IMDs

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CASE HISTORY

A patient who has tried all four atypical antipsychotics

S.S. is a 36 year old female with a 15 year history of mental illness. She was initially diagnosed with bipolar disorder and treated with Lithium. She then developed chronic auditory hallucinations, and her diagnosis was changed to Schizoaffective disorder. She was treated with Lithium and Prolixin (and other neuroleptics) and responded well, but she developed moderately severe tardive dyskinesia, especially tongue and jaw movements. She was then treated with Clozaril, at 400 mg daily for nearly 2 years. Her psychotic symptoms and T.D. almost entirely resolved, but she was often sluggish and fatigued, and she gained nearly 100 pounds. A trial of Prozac was added to Clozaril but was of no benefit with her weight gain. She was slowly switched over to Risperidone at 6 mg daily, but when Clozaril was eventually discontinued, she felt anxious, depressed, and more paranoid, and she asked to resume Clozaril. One year later, she was successfully switched to Olanzapine at 20 mg daily and continued on this Rx for a year. Despite some recurrence of auditory hallucinations and paranoid thinking, she felt less sluggish and lost about 20 pounds, and she was generally pleased with Olanzapine until one year later, when she again developed signs of T.D., notable blepharospasm and facial grimacing. She was switched to Quetiapine and has remained on the medication for the past five months, currently at 400 mg daily. She shows no signs of T.D. at present. Despite ongoing auditory hallucinations, she is able to persevere and maintain functioning. She recently began working in a hospital pathology department as a medical transcriptionist, earning $16 per hour. An avid reader, S.S. has been reading books on the psychoanalytic theory of schizophrenia, and she often astounds her psychiatrist with remarkable insight into her own mental processes.

Psychiatric Medication Management Committee

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3- Acting as an open forum for psychiatrist to seek consultation for difficult or refractory cases.
4- Authorizing the use of controversial medi cines such as Lamictal, Neurontin and newer agents to come.
5- Credentialling psychiatrists and psychologists in our public managed care system.
6- Seeking advice from County Council and disseminating legal information to all psychiatrists.
7- Developing practice guidelines and seeking final approval from the Psychiatric Practices Committee.
8- Beginning collaboration with Stanford Research in recruiting patients for clinical trials.

As we all know, all of us are extremely busy with our work and often feel isolated due to lack of time or availability of our colleagues. The committee is unique in that it is an unparalleled forum for collegial support, interface, consultation, repartee and most importantly fun!

I strongly believe such a committee should be created in any system of care for the mentally ill.

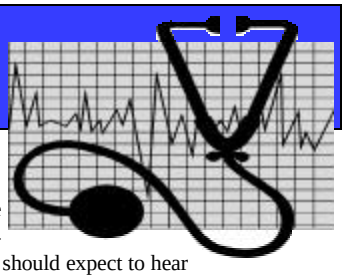
SANTA CLARA COUNTY
GENERIC CLOZAPINE STUDY (Dr. Rothrock's patients)

NAME	AGE	SEX	ETHNICITY	Dx	Rx DOSAGE	BASELINE LABS BRAND CLOZARIL TIME	BASELINE LABS BRAND CLOZARIL LEVEL	FOLLOW-UP LABS GENERIC CLOZAPINE TIME	FOLLOW-UP LABS GENERIC CLOZAPINE LEVEL	TIME DIFF	%CHANGE LEVEL
1	26	M	Japanese	295.30	400 mg HS	11:30 am	160	3:50 pm	142	+ 4 hrs	- 11%
2	45	M	Caucasian	295.30	600 mg HS	12:25 pm	302	11:15 am	533	- 1 hr	+ 76%
3	32	F	Caucasian	295.70	500 mg HS	10:20 am	349	9:30 am	622	- 1 hr	+ 78%
4	39	M	Hispanic	295.90	200 mg HS	11:50 am	466	11:40 am	513	0	+ 10%
5	38	M	Caucasian	295.90	300 mg HS	10:15 am	470	10:20 am	499	0	+ 6%

The chart above contains preliminary data gathered on our first five patients transitioned over to clozapine.

San Francisco County
Community Mental Health Services
The San Francisco Mental Health Plan

FROM THE MEDICAL DIRECTOR...



We recently made some shifts in our pharmacy services to try to reduce the cost of "administration" and make better use of our extremely talented clinical pharmacists. In addition, we have decided to have all reviews of atypical antipsychotic requests for indigent patients ("TAR's" or, now, "PAR's") performed by our in house clinical pharmacists in order to have more consistent criteria for these reviews.

Thanks to very hard work from community advocates, including the Coalition on Homelessness, the San Francisco Medical Society and the San Francisco Psychiatric Society, we were able to convince the Board of Supervisors to provide an additional 1.1 million dollars to help cover pharmacy costs for the San Francisco Mental Health Plan. Unfortunately, costs for atypical antipsychotics are rising at least as fast as we had predicted last year, when we estimated that we could expect atypical antipsychotics for our system to cost nearly 6 million dollars a year within three years.

We remain committed to first line use of atypical antipsychotics, however we have to also be sure that the money that we are spending on these agents is being used wisely. Elsewhere in this letter I outline our partnership with the LASH group and Janssen Pharmaceutica which is working to ensure that as many patients as possible are being made eligible for Medi-Cal. Here I want to note that we are, increasingly, seeing the use of multiple antipsychotic medications in our patients. In many cases this use is appropriate (other approaches have been tried and the patient remains severely symptomatic). In some cases additional agents are being added rapidly, in a way that makes it nearly impossible to figure out what is working and what is not working.

As an example, we recently reviewed a case of a severely ill schizophrenic patient who, over the course of 4 months of treatment, had gotten started on: risperidone, olanzapine (at doses above the FDA limit), quetiapine and depot haloperidol. This patient had reportedly "failed" a trial of clozapine, but had actually never reached therapeutic levels of clozapine. The patient remained severely symptomatic, the medications that this patient was on were costing the system 22,000 dollars a year and nobody could tell what was working and what was not.

Obviously this is an extreme example, but the point

Peter Forster, MD

is that, as we try to understand these medications better, certain basic guidelines exist: (1) these agents generally take a while to work, after reaching a therapeutic dose observe the response for at least 2-6 weeks before increasing doses significantly or adding another medication, (2) single medication trials are generally preferable before trying multiple medications except in severely ill patients, (3) clozapine is significantly underutilized, it is the only medication with an FDA indication for treatment refractory schizophrenia and none of the other agents has yet been shown to share this efficacy.

Our quality improvement staff conduct in depth reviews of certain cases in order to identify areas where our system needs to improve. I would like to share one of the results of that process: we have identified a concern about patients who continue to have the diagnosis of "Psychosis NOS" for more than one year after an initial evaluation. We have seen a significantly higher rates of adverse outcomes in this group, and when we review the charts of these patients we find evidence that the vague diagnosis is tied to vague treatment planning. The classic case is a patient with both substance abuse and significant psychotic symptoms who is probably a substance abusing schizophrenic. The psychiatrist, however, is not sure about the relationship between the substance abuse and psychosis and this uncertainty results in a pattern of temporizing and waiting for things to become clearer. Meanwhile the patient is not getting better. Substance abuse issues are not being vigorously addressed, but neither are the patient's psychotic symptoms, please take special care when you encounter a patient who fits this pattern. As I mentioned before, I am happy to arrange consultation for difficult clinical problems. Call me at (415) 255-3430 if you would like more assistance.

In every mental health system the issue of inpatient to outpatient communication is a thorny one. For the last four months two committees of inpatient and outpatient psychiatrists have been trying to address these issues and come up with some recommendations. You should expect to hear more about our proposals but, for now, we are all agreed that communication between the two doctors, in some form, is the standard of care. Outpatient psychiatrists, please take care to ensure that your answering machines or answering services are setup to assist busy inpatient docs who want to consult with you and don't have more than a day to wait for your response. Inpatient psychiatrists, please routinely leave a message with the outpatient psychiatrist to let them know that you are seeing their patient, and to outline any plans you have for treating that patient. Even a couple of voice mails traded back and forth can make all the difference between good and bad quality care.

I mentioned above that we have developed a collaborative project with Janssen Pharmaceutica and the LASH group to help us ensure that psychotic patients receive Medi-Cal coverage wherever possible. This innovative program addresses one of the major dilemmas facing community psychiatry nationally: the surprisingly low rate of coverage by Medicaid (Medi-Cal in California) for patients with schizophrenia. Given that schizophrenia is a lifelong illness that is almost always associated with inability to work, why is this true? It is, unfortunately, an example of the Catch 22 phenomena: patients can be too sick (too disorganized) to make it through the complicated bureaucracy that administers disability assessments.

With financial support from Janssen, the LASH group will be assisting our eligibility staff to try to "bridge the gaps" and complete all the paperwork needed to get patients onto Medi-Cal or SSI. Please provide all of the assistance you can when you are contacted by the LASH group. If you are contacted, your patient will already have signed a detailed consent form. The LASH group has agreed to keep all but summary information about how well the program works strictly confidential (including from Janssen).

I had the great fortune of attending the private provider (practitioner provider) meeting that celebrated our first year of running the San Francisco

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PHARMACY SERVICES UPDATE

- **CMHS Policy and Procedure 5.00-3**
  A revised version of the CMHS Policy and Procedure 5.00-3, entitled Medical Service Representatives Guidelines / Central Registration / Sample Use, has been finalized. All medical service representatives (MSRs) are now required to annually register with Pharmacy Services prior to conducting CMHS related business. All MSRs will then be given a document acknowledging that they have registered.

  MSRs are also required to submit a presentation report form seven days prior to any group program involving CMHS and CMHS affiliated providers. Both of these steps will enable Pharmacy Services (255-3659) to supply you with MSR contact and event information.

- **Pharmacy Benefits Management**
  CMHS is currently negotiating for a new pharmacy benefits management (PBM) contract. It is through this contract that CMHS' indigent patients are able to go to pharmacies enrolled in the pharmacy network in order to receive their mental health prescriptions. St. Mary Pharmacy Management Services is the current PBM and their contract with CMHS ends September 30.

  Look for upcoming announcements regarding the new PBM contract. If you have any concerns, such as additional pharmacies you would like added to the network, questions about deliveries, prescription forms, etc., please contact Chris Woodside at 255-3703 or Stan Lowe, RPh at 255-3714.

- **AIDS Drug Assistance Program**
  All prescribers should note that there is an AIDS Drug Assistance Program (ADAP) that covers the following antidepressants: Amitriptyline (Elavil), Bupropion (Wellbutrin), Desipramine (Norpramin), Fluoxetine (Prozac), Nefazodone (Serzone), Nortriptyline (Pamelor), Paroxetine (Paxil), Sertraline (Zoloft), Trazodone (Desyrel), and Venlafaxine (Effexor). Prior authorization, by calling 888/311-7632, is required only for Bupropion (Wellbutrin).

  In order to qualify for this program, patients must be a California resident; be at least 18 years of age; be diagnosed with HIV; have a Federal Adjusted Gross Income less than $50,000; and have limited or no prescription drug benefits from another source (not including public assistance).

  Pharmacy Services is in the process of revising the prescription forms for implementation on October 1. The new form will have a bill to box for ADAP. In the meantime, you should note at the top of the current CMHS prescription form "BILL TO ADAP" if you are seeing an ADAP patient and prescribing one of the medications listed above. This will allow CMHS to offset the costs of these medications to ADAP. All of the chain pharmacies and many of the independent pharmacies in San Francisco are participating in the ADAP program.

  To receive more ADAP information, call 888/311-7632 or visit the ADAP website at WWW.PMDC.ORG.

- **EKG tests and interpretations**
  As many of you know, SmithKline Beecham is no longer providing EKG tests and interpretations. CMHS is completing negotiations with another vendor to provide these services. Once negotiations are complete, a letter explaining how to order EKG tests and interpretations will be sent to CMHS providers. For more information, contact Pharmacy Services at 255-3659.

- **$1.1 million increase**
  After a great deal of work and lobbying from CMHS, the San Francisco Board of Supervisors has approved a $1.1 million increase to fund mental health medications for Fiscal Year 1999/2000. This increase will help cover the dramatic rise in medication costs that is being experienced throughout the country.

  This FY, medication costs have increased by 40% when compared with FY 97/8 medication costs. While the number of prescriptions have only increased by 3% when compared to last FY, CMHS prescribers are switching their existing clients over to the newer, more expensive atypical antipsychotic agents that have been found to be more clinically effective.

  Since CMHS experienced a $1 million shortage in medication funds for prescriptions filled through the PBM and for the in-house pharmacy at 1380 Howard, the $1.1 million increase is necessary.

FROM THE MEDICAL DIRECTOR

Continued from page 3

Mental Health Plan. For those of you who are private providers and couldn't make the meeting, let me summarize our discussions. First the good news, we managed to provide a much more accessible mental health service to all indigent and Medi-Cal San Franciscans.

The not so good news is that we have had problems processing claims as quickly as we had hoped. We have renewed our efforts to communicate more effectively with you through our SFMHP Provider Newsletter (please let me know if you are not getting this) and to share with you the problems we have been finding that have been slowing claims payment (wrong procedure codes, wrong diagnosis codes, missing authorizations).

Doctor DeRanieri (Child Medical Director) and I have been working with several quality improvement groups to develop treatment guidelines for our system. There are currently guidelines for treatment resistant depression, atypical antipsychotic use, and treatment of bipolar disorder in youth and adolescence. If you are interested in receiving copies of these guidelines please let me know. We hope to distribute a set of them in the near future.

We have recently been reviewing charts throughout our network and have been impressed with the quality of the care our patients are receiving. However, we have noticed that in a certain number of cases there is not adequate documentation of consent. State law requires written consent for all Short Doyle providers, these laws apply to all providers in our system. If you need a copy of our current consent forms please contact me.

David Hersh, who is the medical director of the substance abuse consultation service for primary care doctors in the Community Health Network recently presented information about guidelines for outpatient detoxification of patients with alcohol abuse and/or dependence. He has indicated a willingness to answer questions by phone for mental health providers. Outpatient detoxification for low to moderate severity alcohol dependence is an accepted procedure that most psychiatrists should be able to manage, Dr. Hersh and his team also have information about other resources that are available for more seriously ill patients. You can reach him directly at: (415)206-5304.

I would appreciate your feedback on this column. Please email me with your thoughts and comments: Peter_Forster@dph.sf.ca.us. Have a great summer!

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1380 HOWARD STREET, SAN FRANCISCO, CALIFORNIA 94103
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San Mateo County
Mental Health Services

THE CUTTING EDGE OF INFORMATION

Barbara Liang, Pharm.D.

After some initial start-up bumps, the Pharmacy Benefits Manager (PBM) program is churning out volumes of valuable data, with the added bonus of significant savings. Being the first county to carve out Medi-Cal mental health medication cost from the State, we are now on the cutting edge of obtaining a comprehensive picture of caring for the mentally ill. In the following sections, I will highlight what we have learned and gained thus far.

Comprehensive Reports

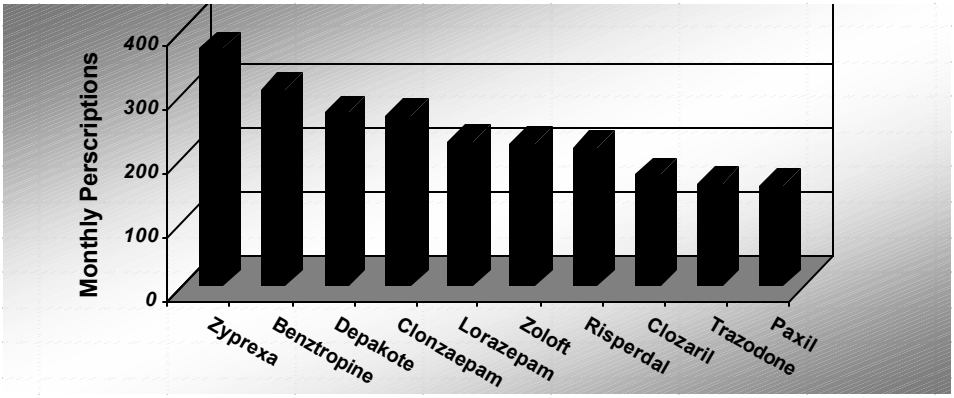
We now receive monthly and quarterly reports accompanied by charts and graphs. These reports, never before available, give us a global view of clients' use of medications, physicians' prescribing patterns, and pharmacies' dispensing activities.

The graphs below show a glimpse of the information available at our fingertips. Top drugs by volume and cost are graphed in a descending order. Atypical antipsychotics rank highest in cost. Zyprexa ranks the highest both in volume and cost. Other high volume categories are benzodiazepines and antidepressants. Of the SSRIs, Zoloft and Paxil are the top runners.

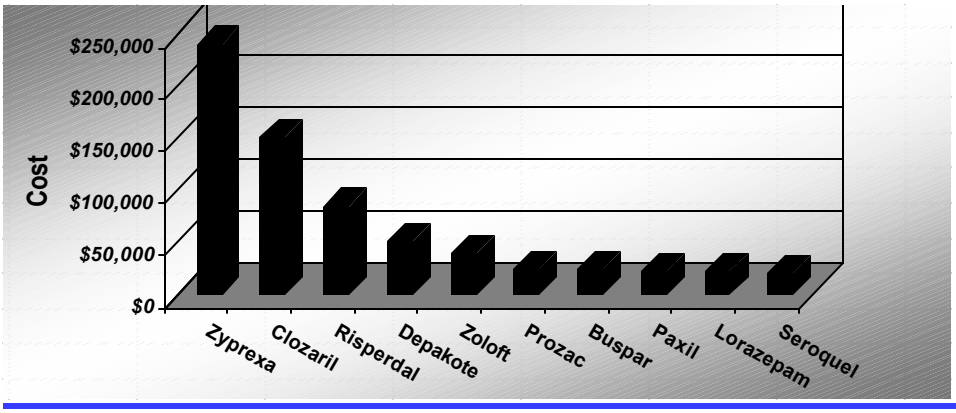
First PBM-assisted Medication Study

In addition to prepared reports, we also receive monthly prescription data on a CD, where we have the ability to design specific queries. Our first endeavor in using this data was looking at young schizophrenic clients and assessing their medication regimens. Given the research about superior outcomes and atypicals antipsychotics in young schizophrenics with first psychotic breaks, Beverly Abbott, Mental Health Director, requested a quality assurance study to evaluate the antipsychotics regimens used in these young clients. The study found encouraging news: the majority (86%) of young schizophrenic patients are being treated with the newer agents. Of the remaining, 4% were prescribed haloperidol decanoate due to noncompliance, 3% had been tried on an atypical and did not tolerate it.

Top Drugs By Volume January 1, 1999 - February 28, 1999



Top Drugs By Cost January 1, 1999 - February 28, 1999



Comparisons

How do the various clients populations compare? Interesting information emerges as we dig a little deeper in the PBM data. For example, looking at the Medi-Cal and indigent populations, we find that on average, more prescriptions are written for the Medi-Cal client (3.8 vs 2.8 prescriptions). Due to the difference in the quantity and type of medications, prescriptions for a Medi-Cal client cost the County 30% more than an indigent client.

How do men and women compare in terms of medication usage? Our data shows female clients were prescribed more medication than their male counterpart (average of 6.1 vs 5.6 prescriptions per client). However, the medications per female client cost 20% less than that for the male client.

Micro View

Not only can the PBM give us the "big" picture of medication usage, it can also "zoom" in on specific treatment issues or geographical locations. Examples of such "micro" views include: usage data on a single agent, drug usage in a diagnostic category, prescription pattern for each clinic, each prescriber, or each pharmacy. The Quality Improvement team will be visiting the managed care physicians in the near future and will provide each prescriber with their own set of data and trends.

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The Cutting Edge of Information

Continued from page 3

Mental Health Computer Screen

How can you access information for your client? Medication data had never before been captured by the Mental Health computer system, but now County psychiatrists can view a client's prescription information on the Mental Health VAX system. The screen is called "PBM EOB Lookup", which lists the dates, medications, and days supply of the prescriptions dispensed by the pharmacies. If you desire this new feature, please request it through Doreen Avery at 573-2284.

Savings? How Much?

Not only has the information been a source of wealth, the PBM has also generated significant savings. This is accomplished by standardizing pharmacy reimbursement rate, as well as reducing duplicate billing, refill-too-soon prescriptions, and inaccurate insurance billing. For the indigent population, the PBM will reduce the annual drug budget by 50%. For the Medi-Cal population, the pharmacy system managed by the PBM will result in 20% savings. Reduced pharmacy cost translates into more funds available for important clinical services, as we strive continuously to better care for our clients.

Future Aspirations

Many other ideas for future medication studies are incubating. Some of these ideas include: clients on multiple medications from the same therapeutic category; average dose of certain medications, such as SSRIs; drug utilization patterns of restricted agents, such as benzodiazepines, naltrexone, nicotine, etc; just to name a few. New ideas to investigate and improve medication use are always welcome, please feel free to contact me or Dr. Bob Cabaj.

We will be working with the inpatient pharmacy to look at the continuity of care, and the usage patterns of certain psychotropics. The next step is to link pharmacy data to that of outcomes research and evaluation, generating the most comprehensive treatment data to date. Armed with this information, we can assess the effect of a clinical intervention or medication on the client's quality of life and on our system of care.

Benzodiazepines and Formulary Changes

Bob Cabaj, M.D.

After the discussion at the last county-wide psychiatrist meeting, the Pharmacy Benefits Management Implementation Committee (which reviews the Mental Health Formulary) reviewed the benzodiazepines currently on the formulary and discussed the clinical use of benzodiazepines.

Though benzodiazepines clearly have a use and are a valuable part of mental health treatment, their high abuse and dependency potential must be considered carefully before they are used. Whether short, intermediate, or long-acting, all benzodiazepines when used at appropriate dosages are equally effective. However, some are more likely to be abused than others - in particular diazepam (Valium) and alprazolam (Xanax). The benzodiazepines used as hypnotics are also all equally effective but the ultra short-acting triazolam (halcion) has particularly troubling side-effects including memory loss, confusion, and withdrawal psychosis. Therefore, the following changes and recommendations have been made and apply to the Mental Health Formulary only (both San Mateo Medical and indigent Mental Health):

- ❖ All prescribers of mental health medications are urged to follow the "San Mateo County Mental Health Services Recommendations on the Use of Psychiatric Medications to Minimize Abuse and Dependency." These recommendations use the "tiered" approach, that is, several steps of interventions before turning to medications that have abuse or dependency potentials. See summary table below.
- ❖ Chlordiazepoxide (Librium, others) is added to the Formulary, in addition to lorazepam (Ativan) and clonazepam (Klonopin).
- ❖ Triazolam (Halcion) is removed from the Formulary.
- ❖ Diazepam (Valium) and alprazolam (Xanax), due to the very high abuse and dependency potential, will now require a Prior Authorization Request (PAR).
  - ◆ For new starts, the PAR will need to document that the step outlined in the attached "Recommendations" were followed first and that the benzodiazepines currently available on the Formulary failed to work.
  - ◆ For long-term users, PARS are still needed since the medications are non-Formulary but will not need these additional clinical justifications. Please make every attempt to switch to the Formulary benzodiazepines.

If you would like a copy of the recommendations in detail, or if you have any questions or concerns, please contact Bob Cabaj at 573-2043 or Barbara Liang at 573-2817.

Summary: **San Mateo County Mental Health Services recommendations on the use of psychiatric medications to minimize abuse and dependency**

Disorders	First Tier	Second Tier	Third Tier
Insomnia	Sleep hygiene	Trazodone Hydroxyzine TCAs	Zolpidem Benzodiazepines formulary, < 2 wks
Chronic Anxiety	Nonpharmacological interventions	Buspirone, SSRIs, TCAs	Benzodiazepines formulary
Acute Anxiety	Propranolol Clonidine Hydroxyzine	Benzodiazepines formulary, < 2 wks	
Panic Attacks	SSRIs TCAs	Benzodiazepines formulary agents	
Major Depression	Psychotherapy	SSRIs, Bupropion Nefazodone Mirtazapine	TCAs
Bipolar	Lithium Valproic Acid Depakote	Carbamazepine Gabapentin	
Psychosis	Atypical Antipsychotics	Clozapine	Traditional Antipsychotics
ADHD in adults	TCAs	Bupropion	Psychostimulants Pemoline

GRAND ROUNDS

Continued from page 1

hol dependence. At the present time, we have good pharmacotherapies for opiates and alcohol but relatively poor treatments for stimulants such as cocaine or methamphetamine.

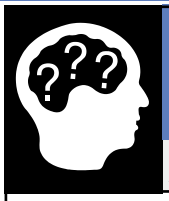
Pharmacotherapy of Psychiatric Disorders

Is it worthwhile to treat psychiatric disorders in patients who are active drug or alcohol users? The answer to this question involves some controversy, but increasing evidence shows that, in particular, treating depression may have beneficial results even among active drug and alcohol users. It certainly lowers depressive symptoms. It is less helpful in actually reducing drug use. Specifically, several studies from the last few years show that using SSRIs or tricyclics can alleviate depressive symptomatology in alcoholics.

Regarding the treatment of other mood disorders, bipolar disorder should certainly be treated even among patients who are active drug and alcohol users. Valproate may be safer than lithium in active drug users. Regarding the treatment of psychosis, again there is clear agreement that pharmacotherapy for psychosis should proceed despite continued drug and alcohol use. Both typical and atypical anti[psychotics are probably safe to use, although the newer medications have an advantage in producing less anhedonia. With respect to anxiety disorders, one would seek to avoid the use of potentially abusable medications like the benzodiazepines. Buspirone (Buspar) is useful and safe for Generalized Anxiety Disorders and SSRIs such as sertraline, paroxetine and others, are indicated for the treatment of panic. Venlafaxine is now indicated for panic and generalized anxiety. For sleep disorders, one would proceed in a step-wise fashion, beginning with medications with low abuse potential such as trazodone or hydroxyzine, and use benzodiazepines only with great caution, if at all.

Conclusion

Most psychiatric medications can be safely and effectively used in patients with drug and alcohol use. However, medications are only a small part of the story with respect to the treatment of alcohol and drug use among patients with psychiatric disorders. Our efforts must go into providing psychosocial treatments for these comorbid conditions. The psychosocial treatments should be, by and large, group treatments and ones that focus on several effective psychotherapeutic "technologies". These involve an emphasis on 1) motivational enhancement through counseling, 2) teaching relapse prevention methods to our patients, and 3) encouraging the use of 12-Step and other self-help programs. The most important take-home point for clinicians is to keep a high level of suspicion for comorbid drug and alcohol problems among psychiatric patients and to aggressively provide both psychosocial and pharmacotherapeutic interventions.



DRUG INFORMATION CONSULTATION

Edited by Renee Williard, Ph.D.

Can bupropion (Wellbutrin) be prescribed with ritonavir (Norvir)?

A theoretical interaction has been noted between ritonavir and bupropion that may result in increased plasma levels of bupropion. The interaction between the two is based on the extensive hepatic metabolism of bupropion and the fact that ritonavir inhibits several hepatic enzymes (CYP1A2, CYP2D6, and CYP3A4). The AUC of bupropion (total amount of bupropion present over time in the body) may increase more than 3-fold due to ritonavir's inhibitory activity on liver enzymes. Because bupropion may lower the seizure threshold, co-administration with ritonavir is generally not recommended. SSRIs as a class would be less likely to interact with ritonavir.

Can you provide me with the latest data on the long term incidence of TD with atypical antipsychotics?

Generally, the annual rate of new cases of TD per year for adults was estimated to be 5% with typical antipsychotics (rates for geriatric patients were much higher). Most initial studies with the atypical antipsychotics were of short duration and did not provide data on the long term incidence of TD. Several studies of one year or greater duration have now been completed. We contacted both Lilly and Janssen to obtain post-marketing data for olanzapine and risperidone respectively.

Lilly estimates the incidence of TD with olanzapine to be 1% based on data from 2500 adult patients treated for approximately one year. Glazer (1997) estimated that, excluding patients who developed dyskinesias within the first 6 weeks of treatment, the incidence with olanzapine was 0.6% per year. Janssen estimates the incidence of TD with risperidone to be 0.4%, based on data from patients treated for more than one year (Brecher, 1996, APA Poster). The incidence in geriatric populations is higher, but still considerably less than with typical agents.

PSYCHIATRIC PHARMACY

Specialization and Board Certification

Talia Puzantian, PharmD

The Board of Pharmaceutical Specialties (BPS) was established in 1976 by the American Pharmaceutical Association (APhA). Its purpose is to recognize specialty practice areas, define knowledge and skill standards for recognized specialties, and evaluate the knowledge and skills of individual pharmacist specialties. BPS has recognized five specialty practice areas in pharmacy: Nuclear Pharmacy, Nutrition Support Pharmacy, Pharmacotherapy, Oncology Pharmacy, and Psychiatric Pharmacy.

Most patient care situations are managed effectively by licensed pharmacists not practicing in a specialty area. Other practice settings, such as psychiatric pharmacy may require specialized knowledge and skills, attained only through additional education and experience. Rigorous certification requirements mean that pharmacists in the defined specialty areas can objectively demonstrate the advanced skills and knowledge necessary to handle difficult and complex patient treatment situations that licensed pharmacy practitioners may not be able to address.

Psychiatric Pharmacy was recognized as a specialty area by the BPS in 1992. The first certification exam was administered in 1996. Since that time, 265 psychiatric pharmacists nationwide have met the requirements for board certification. The specialized psychiatric pharmacist addresses the pharmaceutical care of patients with psychiatric disorders. As a member of a multidisciplinary treatment team, the psychiatric pharmacist specialist is often responsible for optimizing drug treatment and patient care by conducting patient assessments, recommending appropriate treatment plans, monitoring patient response, and recognizing drug-induced problems.

CONTINUING MEDICAL EDUCATION

Doug DelPaggio, PharmD

JUNE 1999	
6/1/99 **12:15 - 1:45 p.m.**	**Managed Care Risk,** *David Sutton, J.D., LCSW* Mills Peninsula Health Services 1783 El Camino Real, Sierra Rooms Burlingame, CA 94010 (650) 573-2530
6/8/99 **12:15 - 1:45 p.m.**	**Gender and Power in Couples Therapy,** *John Niel, Ph.D.* San Mateo County Mental Health Services 225 W. 37th Ave., Multi-Purpose Room, San Mateo, CA (650) 573-2530
6/15/99 **12:15 - 1:45 p.m.**	**Sex and Substance Abuse,** *Robert Cabaj, M.D.* Mills Peninsula Health Services 1783 El Camino Real, Sierra Rooms Burlingame, CA 94010 (650) 573-2530
6/18/99 **12 - 2 p.m.**	**Treatment/medication Compliance Forum,** *SF CMHS Quality Management* 1380 Howard St., 4th Floor Conference Room San Francisco, CA (415) 255-3771
6/22/99 **12:15 1:45 p.m.**	**The Narcissistic Pursuit of Perfection,** *Edward Morehauser, M.D.* San Mateo County Mental Health Services 225 W. 37th Ave., Multi- Purpose Room San Mateo, CA (650) 573-2530
6/25/99 **11:45 a.m. - 1 p.m.**	**Case Conference ,** *Presenter: Dr. James Powers, Discussant: Dr. Mark Levy* San Francisco General Hospital, 1001 Potrero Ave., Room 7M30 San Francisco, CA (415) 206-4938
SEPTEMBER 1999	
9/16/99 **6:30 p.m.**	**Bipolar Disorder,** *Mark Frye, M.D.* CMH 1380 Howard St., San Francisco, CA (415) 255-3703

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