

The New Generation of Medications Available for Psychiatric Disorders

Summarized by Thomas T. Thomas

The drugs available to treat brain disorders like schizophrenia and depression are constantly changing and improving. The Food and Drug Administration has recently approved several new medications in two areas of interest to our members: atypical antipsychotic drugs and serotonin selective reuptake inhibitors (SSRIs).

At our March 25 meeting, **Gary Viale, PharmD**, returned to discuss the most recent crop of medications. (He was our speaker on this subject in September 1995.) Viale is Assistant Director of Pharmacy at the Santa Clara Valley Medical Center. He was instrumental in convincing Santa Clara County Mental Health to approve the newer, more costly medications for schizophrenia on the grounds that they reduce hospitalizations and thus reduce the overall cost of treatment. Many of our members also know him from the popular brochure "Medications for Mental Health," written with Carole Calkins, PhN.

Joining him was **Douglas Del Paggio, RPh, MPA**, Director of Pharmacy Services for Alameda County's Behavioral Health Care Services, our local mental health agency. Both Viale and Del Paggio are Assistant Clinical Professors of pharmacy at the University of California, San Francisco.

"This is a very exciting time in psychiatric pharmacy," Viale said, "both with new medications becoming available and with new ideas developing about the older medications."

He noted that organizations such as ASA-AMI are having an effect in the field, too. If not for their advocacy, three of the newest antidepressants and four antipsychotics would not be on the Medi-Cal formulary.

"Thanks to groups like this," he said, "Santa Clara Valley's budget for mental health medications is growing by \$100,000 a month." But the cost of the newer medications—although they are more effective, present fewer side effects, and help avoid costly hospital stays—is also rising.

Viale explained that, while the older drugs to treat mental illness might cost on average \$87 a year, the newer antipsychotics cost \$2.80 to \$7.80 a tablet. So a year's worth of medication might run \$3,500 to \$7,000 per patient. And Santa Clara provides these medications without considering the patient's ability to pay. "Anyone can get them," Viale said.

Del Paggio, who has been in his position with Alameda County for two years, and six years before that at St. Francis Hospital in San Francisco, said the county tries to evaluate all the medications available to their psychiatrists. He also agreed with Viale that it's an exciting time to work in psychopharmacology.

"After years of fairly standard medications for mental illnesses like schizophrenia," Del Paggio said, "Prozac came along and broke new ground. It

showed the pharmaceutical companies that they could make money here. Now more medications are being tested and coming to market than ever before.”

These drugs, he said, treat symptoms the old ones do not address, and they have a cleaner adverse-effects profile. That means it’s easier for patients to stay with the new drugs and keep taking them longer. Patients are getting better, so agencies like Behavioral Health Care Services are experiencing a paradigm shift: they have to plan for the reintegration of their clients into the community.

Del Paggio said that, with the new medications, patients undergoing a first psychotic break are not developing chronic symptoms, and established patients who have not responded to the older medications are also improving with the newer drugs. “It’s important for us to keep monitoring patients and their medications to see how they respond. If one is not working, maybe something else will.”

Viale added that the current trend is to try a “cocktail” of these drugs—instead of the psychiatrist’s traditional method of picking one medication and sticking to it. (Both Viale and Del Paggio, however, were adamant about mixing medications with alcohol and marijuana: it’s a bad idea. Substance abuse only scrambles the conditions the medications are trying to treat, they said.)

Del Paggio went on to say that we now know more about schizophrenia than ever before. The consensus among the medical community is that this is not a single illness but a group of related conditions. Every patient presents with a unique combination of symptoms.

He described the positive symptoms—delusions, hallucinations, paranoid thoughts—and said the older generation of antipsychotic medications like Thorazine and Prolixin tend to treat these symptoms well. But these more obvious symptoms of the disease also tend to decrease over time.

The negative symptoms of schizophrenia—disorganized thought and speech patterns, impaired memory and judgment, loss of drive, loss of expressiveness, lack of enjoyment—really affect the personality. These are the symptoms that older drugs treat less well, but the newer “atypical” medications like Clozaril, Risperdal, and Zyprexa do much better.

“The negative symptoms appear as soon as the patient starts to get ill, often before the first psychotic break,” Del Paggio said. “Also, these symptoms tend to get worse over time, not better. The atypical drugs can keep these symptoms from appearing, although they may not replace whatever cognitive function has been lost.”

Del Paggio spoke of the problem of co-morbidity—or the tendency of patients to present with more than one mental illness. Depression, anxiety, suicide, and substance abuse are common in schizophrenia, he said. Ten to thirteen percent of schizophrenics commit suicide. Fifty to eighty percent abuse alcohol or street drugs.

“That’s one of the reasons the Food and Drug Administration has put these newer psychiatric medications on fast-track approval,” Viale added. “The government finally woke up to the fact that you can’t afford to do nothing.”

Del Paggio described another paradigm shift, this one resulting from the medical community’s deeper understanding of schizophrenia’s symptoms.

All activity in the brain depends to some extent on the class of chemicals called neurotransmitters. These substances carry the message from one brain cell to another. Psychiatric medications work by altering the way the brain's various neurotransmitters are produced, released by the source cell, received by the target cell, how the excess is handled, and how the chemical is reabsorbed by the cell or metabolized.

One such chemical is dopamine. This substance is produced in the brain stem and has many functions: it is associated variously with the brain's activation and reward system and with motor control or movement. Another neurotransmitter is serotonin, which regulates hunger, pain, aggression, sex drive, emotions, and sleep patterns.

The old paradigm focused on blocking or augmenting these neurotransmitters. Blocking them calms the positive symptoms of schizophrenia, but it can also dull the patient's mood and, in the case of dopamine, cause Parkinson-like motor problems, such as tremors, disjointed movements, and stiffness. Augmenting these neurotransmitters treats most kinds of depression, but it can also cause nervousness, nausea, constipation, and insomnia.

The newer atypical medications instead work according to the hypothesis of "dysregulation." This says that conditions like schizophrenia or depression are caused when the production, use, or metabolism of these neurotransmitters gets out of balance. Instead of blocking or augmenting production of the neurotransmitter entirely, these medications work selectively to block its reception. That is, they keep some but not all of the brain's centers from using a particular neurotransmitter if too much happens to be available. Or they increase receptor sensitivity if too little neurotransmitter is being released by the source cell.

Therapies using a combination of these drugs—or "cocktails"—are possible, Viale noted, because each medication blocks reception of a particular neurotransmitter in a particular part of the brain.

In the end, Viale and Del Paggio urged psychiatrists, their patients, and the families involved with them to stay informed about the newer medications.