

A Review of Psychotropic Medications

Summarized by Thomas T. Thomas

The speaker at our September 2011 meeting was Dr. Dri Wang, one of three clinical psychiatric pharmacists with Alameda County Behavioral Health Care Services (ACBHCS), an organization encompassing 32 outpatient mental health programs. Dr. Wang completed her specialty psychiatric pharmacy residency at the University of Southern California and worked in settings such as Los Angeles County's inpatient and outpatient mental health facilities and its psychiatric emergency service. She treated mental health outpatients at a primary care site in LA's "skid row" district, and has also served as a psychopharmacology educator. Her talk at NAMI East Bay focused mostly on antipsychotic medications.

These medications treat psychosis, which is a symptom of many illnesses described in the *Diagnostic and Statistical Manual* (DSM-IV) like schizophrenia, schizoaffective disorder, and acute mania. They also help in maintaining patients with bipolar disorder and treat aggression and agitation.

"No one knows exactly what's going on in the brain," Dr. Wang said, "so theories about schizophrenia have evolved over time. Now people think the disease is due to a chemical imbalance." Four key brain chemicals seem to work in concert, and the levels of any one seem to affect the others:



DRI WANG, PHARM D

- **Serotonin**—governing mood, appetite, sleep, learning ability, and the sense of well-being.
- **Dopamine**—affecting motivation, reward, and physical movement.
- **Norepinephrine**, or adrenaline—governing the fight-or-flight response to threatening stimulus.
- **Glutamate**—a master on-off switch that appears to govern levels of the other three chemicals.

The current paradigm for schizophrenia suggests that too much dopamine in the mesolimbic cortex leads to hallucinations and delusions, while too little dopamine in the frontal lobe affects executive functioning. Thorazine[®],¹ introduced in 1955, and other first-generation or "typical" antipsychotics block dopamine in the brain. While this reduces delusions and hallucinations, it also leads to the movement disorders seen in old movies about psychiatric wards, such as muscular rigidity and stiffness, shuffling gait (pseudo-Parkinsonism), and restlessness (akathisia), collectively known as extrapyramidal side effects (EPSE).

¹ For complete information on psychotropic medications and their effects, see go to the ACBHCS Medication Consent Form & Drug Information, www.acbhcs.org/meddir/consent.htm.

Prolonged use of the first-generation medications can lead to tardive dyskinesia (TD), characterized by involuntary facial and arm movements. TD is irreversible unless caught early, and so use of the typical antipsychotics is paired with regular tests on the Abnormal Involuntary Movement Scale (AIMS) to guard against this condition. It's thought that dopamine receptors blocked for a long period of time, as with continued use of these medications, will "up regulate" and become more sensitive to dopamine.

In the 1990s, second-generation or "atypical" antipsychotic medications like Clozaril[®] and Risperdal[®] began appearing. They greatly reduced movement side effects. When Zyprexa[®] appeared in 1996 it was met with great enthusiasm, but then patients began experiencing metabolic dysfunctions like abnormal weight gain, high cholesterol levels, and diabetes—and sometimes diabetes preceded the weight gain, which is not the usual pattern seen in the antipsychotic-naïve population. The medications with the most metabolic side effects are Clozaril, Zyprexa, and Seroquel[®]. Dr. Wang noted, however, that every patient's brain chemistry is different, and some patients do well on these medications without weight gain.

Some of the antipsychotic medications that have recently been FDA approved include:

- **Invega[®]** (generic: paliperidone) came out at approximately the same time Risperdal went off-patent. Invega is a metabolite of Risperdal—that is, while the latter only becomes active through changes inside the body, Invega is the active form ingested as a tablet.
- **Sustenna[®]** (generic: paliperidone palmitate) is similar to Risperdal Consta[®] as an injectable form, which is better for medication compliance, because the patient takes it every few weeks. For Consta the interval is two weeks, while for Sustenna it's four weeks.
- **Saphris[®]** (generic: asenapine) was approved by the FDA in August 2010 as the first antipsychotic that's taken under the tongue. Administered twice daily, doctors like to use it in hospital settings because the medication is absorbed before the patient can "cheek" the pill and dispose of it later. Saphris has similar efficacy to Haldol[®] but with lower EPSEs. However, the FDA has issued a warning about severe allergic reactions with Saphris, including rashes, throat swelling, respiratory distress, and anaphylaxis.
- **Fanapt[®]** (generic: iloperidone) went into clinical trial a decade ago in comparison with Risperdal, but it took longer to reach titration (i.e., effective concentration) and did not show equal efficacy. Another company recently bought the rights and tested it effectively against Geodon.
- **Latuda[®]** (generic: lurasidone) is a good dopamine blocker with not as much weight gain. It also appears to have the least cognitive, or memory, impairment of all the antipsychotics.

Dr. Wang noted that the atypical Clozaril (generic: clozapine) has been demonstrated as the most effective against treatment-resistant schizophrenia. "However, medications that are most effective tend to have the worst side effects," she said. Clozaril's include weight gain, heart problems with symptoms similar to heart failure, and reduced white blood cell counts. These side effects

tend to show up in the first month; so patients need regular blood tests with increased frequency during early stages of use.

She also noted that clinical trials often compare a medication's effectiveness to the placebo to obtain FDA approval. Few studies compare one antipsychotic versus another in head-to-head trials.

The future of antipsychotic treatment, Dr. Wang said, appears to be regulation of glutamate. She noted that the effects of the street drug PCP ("angel dust") are identical to the symptoms of schizophrenia, and that PCP affects the glutamate system. Successful treatment with glutamate to restore chemical imbalance may still be a couple of decades away.

Dr. Wang noted that a patient's social support from family and peers and lack of stress in the environment have a powerful effect on symptoms. A patient who is doing well on medication may have a relapse if the personal situation changes and stress levels increase. "No medication works perfectly or for all time," she said. "There is no magic bullet."

At this point, Dr. Wang took questions.

Q. What do you think about drug cocktails?

A. If a second-generation medication is not working, then you might supplement it with a small dose of a first-generation. But there's no proof that two medications work better than one. We prefer a single therapy and require documentation for additional medications.

Q. What causes drug interaction side effects?

A. The liver cleans all medications, as well as other substances, from the bloodstream. If one substance blocks a chemical pathway in the liver, it can lead to increases in concentration of other substances that use that pathway. For example, you're not supposed to take Lipitor[®] with grapefruit juice, which blocks the medication's elimination pathway and causes a buildup. Sometimes, also, medications simply have the same side effect. For example, both the antidepressant Prozac[®] and aspirin or ibuprofen thin the blood, so taking the two together may increase the potential for stomach bleeding.

Q. Does psychosis ebb and flow with time, and can it eventually go away without long-term medication?

A. Sometimes people with borderline personality disorder—"borderline" meaning on the border of psychosis—can exhibit symptoms of psychosis. These may be people with histories of emotional neglect, trauma, abuse, and comorbid substance abuse, who easily become aggressive and exhibit emotional lability. They sometimes are misdiagnosed as having schizophrenia, schizo-affective disorder, or bipolar disorder. These patients may stabilize without medication but with intense therapy.

Q. What are your thoughts on a recent study showing patients do better in third world countries without medication?

A. One theory says that these countries tend to have good peer support and lower stress levels. But some countries treat mental illness as demon possession, caging and chaining up people. Psychotropic medications are not as perfect as the pharmaceutical companies sometimes suggest, but they do allow people to lead better, more productive lives.