SPEAKER NOTES

Psychotropic Medications: What's on the Horizon?

Summarized by Thomas T. Thomas

New medications will become available this year that not only have fewer side effects but may also treat a wider range of symptoms. The speaker at our January 26 meeting, **Mark Watanabe, PharmD, PhD, BCPP,** Assistant Director of Pharmacy for Alameda County Behavioral Health Care Services, gave us an overview of what's available and what's coming.

DR. MARK WATANABE

Dr. Watanabe is new to Alameda County, coming to us in June 1999 after filling a similar position in Illinois. As a clinical pharmacist specializing in psychiatry, he facilitates access to psychotropic medications—which can be very expensive—for the agency's clients, who are generally in the lower socioeconomic class. He also consults on these medicines with the county system's psychiatrists, a duty which includes monitoring lab tests and reviewing side effects.

"The older drugs," he said, "had lots of side effects, often as many side effects as they had therapeutic effect. Then in the late 1980s three drugs became available—Prozac for depression, Buspar for anxiety, and Clozaril as an antipsychotic—which were more selective in treating symptoms and so had fewer side effects." Dr. Watanabe was personally involved in early studies with Clozaril and became excited by the possibilities represented by these new medications.

The newest antipsychotic on the horizon, he said, is Zeldox (generic: ziprasidone) from Pfizer. The Food and Drug Administration is studying it for possible effects on the heart, but after that it should be available this fall. Zeldox shares properties with the neuroleptics Zyprexa and Risperdal for reducing hallucinations. It also has some antidepressant properties, so it may be useful in more than one area. The main side effect is sedation. And unlike Zyprexa, which has the properties of an antihistamine, Zeldox does not seem to cause weight gain.

Dr. Watanabe said that for immediate relief of psychotic symptoms, these medications can be injected. So far, only Haldol (generic: haloperidol) is available in injectable form, but Zeldox may also be made available as an injectable.

Another new medication, due out in the spring from Pharmacia & Upjohn, is Vestra (generic: reboxetine), which is indicated for depression. Many antidepressants target the serotonin system, he said. Some of the newer medications, like Effexor (generic: venlafaxine), also go after norepinephrine in the brain. Vestra treats norepinephrine solely, so it will offer patients another

medication which avoids the side effects associated with serotonergics like Prozac, Paxil, and Zoloft.

After this brief introduction, Dr. Watanabe took questions from the audience.

Can medications that are useful for depression also be used for bipolar syndrome?

Yes. However, some of these medications—for example, the tricyclics such as Elavil (generic: amitriptyline)—when administered for depression give the patient an energy boost which can make him or her manic. So it's important with bipolar to take a mood stabilizer along with the antidepressant to avoid switching over.

Some symptoms may be present in various illnesses. For example, thought disorders and hallucinations are not just symptoms of schizophrenia but may also occur in depression. So, in the initial stages of treatment, the psychiatric pharmacist may identify target symptoms and attempt to treat them with two or more medications. But over the long term the primary symptoms of the illness will become clear—either depression or psychosis—and then the doctor will phase out other medications.

"Family members can help identify these long-haul symptoms," Dr. Watanabe said. "You can describe what you see and what's going on with the patient."

Are brain scans useful in treating mental disorders?

They are helping us learn more about the mechanism of the illness. It is also possible to give a patient a dose of medication and put him or her inside a magnetic resonance imager (MRI), which will show some of the medication's immediate effects on the brain. But brain scans are not clinically practical for diagnosis.

What can we do about toleration for a medication, when the effectiveness wears off? What about age and toleration?

Toleration seems to depend on the frequency of the patient's episodes. Each one reduces his or her chance of returning to a baseline state. We don't have much data on antipsychotic medications, but antidepressants like Prozac, Paxil, and Zoloft can lose their effectiveness. When medications suppress the availability of neurotransmitters, the brain's synaptic receptors sometimes—although relatively infrequently—can react by multiplying and so countering the effects of medication.

Most medications are broken down in the liver and excreted by the kidneys. Young people tend to have very efficient livers, so they may need a higher dosage to get an effect. Older people tend to have reduced liver function, so they should probably cut down on the dose.

What is the recommended period for changing from one medication to another?

In the initial period of treatment, the patient needs an "adequate trial" with the medication—at least six to eight weeks at a dose that falls within the therapeutic range for most patients, according to tables provided by the manufacturer. When switching to a new medication, you should taper off the old one to avoid withdrawal symptoms, especially with drugs that affect receptors in

the brain. This tapering period should last about one to two weeks; then the patient begins with the new medication at the regular recommended dose.

All medications have a "half-life," which represents the time for the amount in the system to drop by 50 percent after the patient stops taking it. For example, Risperdal has a half-life of 12 to 24 hours. So it takes about a week, or five half-lives, to wash it effectively out of the system.

What medications are available for bipolar syndrome?

Lithium is the gold standard. However, it can be tricky to use and requires blood tests to monitor levels in the body. About 70 percent of patients respond to lithium, but about 30 percent don't. Tegretol (generic: carbamazepine) helps patients who don't respond to lithium and also works for patients who are rapid cycling, with up to four episodes per year.

Depakote and Neurontin were introduced as anticonvulsants, to treat seizure disorders. They also work for manic and impulsive behaviors. The therapeutic model is that these behaviors share the same irritable focus in the brain that is subject to electrical misfires during *grand mal* seizures.

Zyprexa can also be used to treat manic behavior as well as thought disorders.

How concerned should we be about drug interactions?

Tegretol speeds up liver enzyme function and thus can break down large doses of Zyprexa. So, when taken together, they may reduce the latter's effectiveness.

Should we be concerned when the doctor recommends medications for other illnesses?

Prescribing "off label," as it's called, is not improper or illegal. The Food and Drug Administration requires the manufacturer to conduct clinical trials to show safety and efficacy for a single indication or illness. The manufacturer cannot claim that the medication will treat other indications. But the physician, who is following the literature in the field and heeding warnings about drug interactions, is permitted to prescribe for other illnesses.

What about administering psychotropics to children?

These medications are usually prescribed for children 12 and above, so there is not a lot of information on younger patients. We have learned that children are not just small adults. For example, their higher metabolisms means that they can tolerate and may need larger doses than adults. However, because of legitimate concerns, the FDA is very conservative about granting approval of clinical trials with children.

What are the effects of gastro-esophageal reflux disorder (GERD or acid reflux)?

Prilosec (generic: omeprazole), which is commonly prescribed for this condition, seems to inhibit the liver enzymes that metabolize drugs. So Prilosec would tend to elevate levels of drugs like Risperdal (generic: risperidone) and thus increase the risks of toxicity and adverse effects. However, no clinically significant drug interaction between omeprazole and risperidone has been documented. There are other acid-reducing medications the patient can take and other treatments to try.

Have genetic studies been done about patients' reactions to drugs?

Yes, relating to drug metabolism. Certain people don't produce some liver enzymes as well as others. So, for some medications, they can do just as well on a lower dose. There are also gender or hormonal differences that affect dosing. And, as indicated above, age is a factor in toleration.