SPEAKER NOTES

Local Research on Bi-Polar Disorder and Major Depression

Summarized by Thomas T. Thomas

A private psychiatrist with a practice in the East Bay, **Randy Bloch, MD,** is involved with research on medications for schizophrenia and schizo-affective disorder, bi-polar disorder, major depression, social phobias, and other psychiatric and neurological diseases. Dr. Bloch runs the Affiliated Research Institute (ARI) in Lafayette, California, which participates in clinical trials on both an in-patient and out-patient basis for pharmaceutical companies. At our January 23 meeting, he discussed some of the new medications becoming available for these brain malfunctions.

RANDY BLOCH, MD

"Currently, we are doing a double-blind study on Seroquel Extended Release," he said. "Seroquel is an antipsychotic medication with fewer extrapyrimidal side effects—such as muscle stiffness and tardive dyskinesia—than Risperdal or Zyprexa. But Seroquel does require dosing twice a day, which raises the problem of patient compliance. The Extended Release formulation under study would only have to be taken once a day." ARI is one of 30 sites around the country participating in this study, which has been going on for almost a year.

All the patients in the study are volunteers and all have schizophrenia. Dr. Bloch establishes this diagnosis by an interview with the patient, examination of his or her medical history, and corroboration by family members. The patient cannot participate if he or she is on Clozaril or is treatment resistant. "There are different types of schizophrenia," Dr. Bloch says, "and schizophrenia and schizo-affective disorder are not clearly distinguished. We cannot, for example, take patients who have any symptoms of bipolar disorder."

The patient is admitted to the hospital for ten days and taken off any current medications. The patient is put on Seroquel Extended Release at one of a number of fixed dosages, such as 600 or 800 milligrams, or on the placebo. The doctor can only alter the dosage to reduce it if there are side effects. As the study is still ongoing, there is no report as yet on the effectiveness of the Extended Release formulation.

"We are also doing several studies on depression," Dr. Bloch said. "Some are in Phase IV, which is after the drug reaches the market." Clinical trials of medications go through several phases. Phase I includes test tube studies to establish a drug's pharmacodynamics and pharmacokinetics (i.e., how it seems to

work) and safety trials with animals. In Phase II, a group of healthy people take the medication to show that it is safe for humans. In Phase III, several thousand patients with the established disease indication take the medication against a similar control group which is taking a placebo. (The trials are called "double blind" because neither the doctor nor the patient knows who gets the medication and who gets the placebo.)

"In one trial for depression," he said, "we are testing Remaron, a medication that has been available in Europe for 10 to 15 years and in the U.S. for less time. This is a dissolvable tablet, which is easier for older people to swallow. Remaron is intended for people with the type of depression that involves not eating or sleeping well. In another trial, we are testing Gepirone, which is for atypical depression, where people are overeating and sleeping too much.

"With both of these trials," Dr. Bloch said, "the medications are not necessarily better than existing treatments, but they work better for a certain kind of person with an particular form of the disease. This is the nature of modern drug development: subtyping patients with special groups of symptoms and finding medications that work best for them."

At this point, the doctor took questions from the audience.

Do you use scanning techniques in the Seroquel trial?

We don't use scanning—such as magnetic resonance imaging (MRI) or positron emission tomography (PET)—because Seroquel does not bind as closely to dopamine receptors.

In your studies with schizophrenia, how do you measure progress?

We have a clinician administer the Positive and Negative Symptom Scale test (PANSS) during an interview. This is common in all clinical trials with schizophrenia and elicits information from the patient that maps his or her symptoms.

Do the clinical trials you are working on apply to children, or young people pre-puberty?

No. The developing brain is different from the developed brain, and this has been a problem with past trials. The Food and Drug Administration (FDA) has ruled that medications which might be used in treating children must have special studies done. But it is difficult to get parental consent to volunteer children for double-blind studies, where the patient might be in the control group and treated with a placebo.

When a young person is put on antidepressants and told he or she has to take them forever, what are the long-term side effects?

First, medication is not the only potential treatment for depression. Psychotherapy, such as cognitive and interpersonal therapy, has been shown to be just as effective for some people. Second, many young people have emotional states including attention deficit disorder (ADD) and often "act out." It is difficult to distinguish these problems from patients with true depression.

Of the available medications, however, Prozac and similar serotonin selective re-uptake inhibitors (SSRIs) have been on the market since the late 1980s and in clinical trials since the mid-1970s. So we have patients who have been taking them for about 25 years. These medications seem to be relatively safe, even for women during pregnancy.

Are you doing any studies on depression with psychosis?

Not at ARI. These patients are hard to find, because less than 5 percent of people with depression exhibit symptoms of psychosis.

There is a doctor at Stanford University who is working with RU-486 on psychosis. This is the "morning-after" abortion pill, which is a steroid blocker in the brain: by blocking progesterone, it causes uterine contractions and abortion. People who have taken a lot of steroids may become psychotic; so the direction of this research is to see if RU-486 can be used to rapidly reverse psychotic symptoms.

My daughter has bipolar disorder with attention deficit hyperactivity disorder (ADHD). Will she have to take medications for the rest of her life?

We believe bipolar disorder can be controlled but not cured. However, there is some evidence that if you can catch it early and avoid major manic episodes by taking medications such as lithium and Depakote, the patient will have a better long-term outlook. Bipolar is characterized by cycles, and you have to change the dosages over time. During the manic phase, a patient will metabolize medications much faster, so you have to give them more to maintain the therapeutic effect.

Certain drugs, especially those for acquired immune deficiency syndrome (AIDS), have been fast-tracked by the FDA. What about doing this for medications that treat mental illness?

The FDA does a cost-benefit analysis when approving drug trials. If the disease to be treated is fast and fatal, the regulators will speed up the trial period. Development and testing are usually slower for mental illnesses. Because these medications are taken for long periods of time, the FDA wants to avoid introducing medications that may have toxic side effects.

Is there any herbal treatment that helps bipolar patients in their manic phase?

There is some data to support the idea that Omega III fatty acids, such as found in salmon and some other fish, will help with bipolar disorder. The studies that have been done indicate that you have to take about 9 grams a day, which is equivalent to eating a whole big salmon, and there may be cardiovascular effects at this dosage. But there are no herbal supplements for bipolar.