SPEAKER NOTES

Current Psychiatric Thinking and Research

Summarized by Thomas T. Thomas

A general psychiatrist with Berkeley Mental Health on the front line in dealing with clients and families, as well as an active member of the local American Psychiatric Association, **Dr. Jeffrey Johns** spoke at our March 24 meeting. He gave us an overview of the current thinking and research in psychiatry and answered members' questions.

In addition to his work at Berkeley Mental Health, where he has practiced for two years, Dr. Johns spends half his time in private practice in the Rockridge section of Oakland. Before that he was in the U.S. Air Force as a psychiatrist at Travis AFB.

DR. JEFFREY JOHNS

Some of the trends he has observed include:

- Not many new psychiatric medications are coming out now, and none is revolutionary. The current medications will be with us for some time.
- Articles in the media are beginning to cast doubt on the effectiveness of some of the medications, especially the antidepressants.
- We are hearing more about the negative side effects of many medications.
- The American Psychiatric Association is currently preparing the successor to the *Diagnostic and Statistical Manual of Mental Disorders IV, Text Revision (DSM-IV TR),* which is the "bible" for professionals in the field. The new fifth edition will not appear until 2012, and the APA is soliciting input on the internet at the site http://www.psych.org/MainMenu/Research/DSMIV/DSMV.aspx. This is our opportunity to see what they're thinking and offer comment.

After this brief introduction, Dr. Johns opened the meeting to questions.

Q. NAMI is trying to make anosognosia—lack of insight into the fact that one is ill—a diagnostic for mental illness. How does the medical community get people to stop denying they're sick?

A. That's a tough issue. Lack of insight is very common to both bipolar disorder and schizophrenia, and it's an obstacle to treatment. Sometimes the psychiatrist can involve the patient with different people he or she knows and trusts, and if they're all saying the same thing, it can have an effect. Another approach is to focus on what the patient wants, rather than on what we think he or she needs. So if he wants to stop suffering, to be out of pain, you offer options for treatment, and he will slowly develop an understanding of the illness.

Q. Do street drugs like methamphetamines cause mental illness?

A. That goes to the core question about the disease, and it's very complex. Street drugs can cause psychotic symptoms such as hearing voices and having hallucinations while someone is intoxicated. But these effects do not usually last when the person becomes sober. So the simple answer is, no. But some people can

still experience effects shortly after they stop using. And teenagers and young adults who are heavy cannabis users do increase the risk of developing schizophrenia. The scientific evidence is not good enough to say that marijuana is a cause. Schizophrenia may be caused by multiple factors such as genetics and the environment—and drug use is part of the environment. Current thinking is that drug use may be a trigger if the patient has a propensity toward the illness.

Q. Are schizophrenia and bipolar disorder on a spectrum?

A. We think of them as distinct. But again, it's not quite that simple. Schizophrenia involves delusions, hallucinations, paranoia, and illogical thinking and behavior. It's a chronic illness that waxes and wanes. Bipolar has a spectrum of severity. In its severe form, the illness involves changes in mood, from happy or angry periods called mania that last about seven days, during which the patient may do dangerous things like overspending and having sex with strangers, then into a deep depression. This swing may happen once in a lifetime or several times a year. The swings may be mild or severe.

However, *DSM-IV* identifies schizo-affective disorder as schizophrenia with depression or schizophrenia with bipolar disorder. So the two diseases can coexist. The more we know, the more we think the distinction may not be as clear as we thought. For example, genetic studies have shown that if you have a family member with bipolar, you're more likely to have schizophrenia than chance would suggest, and vice versa. Clinical studies suggest that the same doctor might diagnose differently—either schizophrenia or bipolar—based on how the illness is presented. And there are indications that schizophrenia itself may be multiple diseases.

Q. Are people still diagnosed based on their response to certain medications? Now that we have more finely tuned medications, is the picture no longer so clear?

A. For a long time we had silos. Lithium was the first medication identified for bipolar disorder, and it was used to separate out the illness. And then we had Depakote (generic: divalproex sodium). For schizophrenia, we had Thorazine (chlorpromazine) and Haldol (haloperidol), and then we added the various antipsychotic medications. The more we learn about these illnesses, the more we also learn about the effects of the medications.

Q. How long does it take for lithium to have an effect on bipolar?

A. That's hard to say. If the patient is at the full dose for lithium and has another manic episode, it's time to try something else in addition to the lithium. Note that lithium is a potentially dangerous drug. So if it's not working, try something else.

Q. Why aren't there more new medications? Why is there no research.

A. It's not for lack of money. The drug companies simply haven't had much luck with new compounds. Back in the 1960s we developed animal models for drug research. More recently, we've developed genetic studies and stopped using the animal models—and since then we haven't found much new. People are now looking at the causes of disease through new methods such as epidemiology, genetics, and brain scans. We simply have a tough time defining the mechanisms of mental illness.

Q. Is any research being done on cerebrospinal fluid and neurotransmitters.

A. This is a big issue. For twenty years we've known about dopamine and serotonin. And the current thinking is that schizophrenia is caused by dopamine levels being too high, while depression is caused by serotonin levels being too low. We have drugs that have been developed based on these theories, and the theories were developed based on the actions of the drugs. But the truth is, we don't have good scientific evidence to support either theory.

Q. I've read about a new antipsychotic medication called asenapine (Saphris), and the study says it has more impact on the negative symptoms of schizophrenia than Risperdal (risperidone).

A. Saphris has been around a while. It's been used in Europe for schizophrenia and was recently approved for the American market. I haven't seen it in action. Another new medication is Fanapt (iloperidone). I'm not impressed with these medications. The literature suggests that neither of them is much better than the placebo for dealing with the *negative* symptoms of schizophrenia—the loss of interest and flat affect—rather than with the more florid symptoms like psychosis. The drug companies are very creative in comparing drugs for the negative symptoms. But the newer atypical antipsychotics like Zyprexa (olanzapine), Abilify (aripiprazole), and Geodon (ziprasidone) are really no better for the negative symptoms than Haldol.

They may not even have fewer side effects, just different sets of risks. The newer drugs like Seroquel (quetiapine), Clozaril (clozapine), and Risperdal simply haven't been out as long. And some of them have been shown to cause diabetes, heart attacks, and strokes. Abilify, which is from the same family, is not as likely to cause the weight gain and diabetes—but it is more likely to cause tremors and restlessness.

Lamictal (lamotrigine) is best classed as a mood stabilizer for bipolar disorder along with Depakote and lithium. Lamictal is mild in its side effects and is better at treating depression than mania—but the side effects include a rash than can slough off your skin and kill you.

Ultimately, you have to examine the whole arsenal and find the right medication for the individual patient.

Q. How do you treat bipolar type 2,which has major depression but with less severe mania?

A. There are not many studies on this. Generally, we use the same medications as for bipolar type 1. There's a major controversy as to whether we should use an antidepressant. Antidepressants have not been shown to help and may trigger a manic episode, although that's not been proven clinically. If someone has bipolar, is taking a mood stabilizer, and is still depressed, you might try a low dose of antidepressant. Abilify is often added to treat bipolar depression. For some people it acts like a sedative and in others it can cause restlessness.

Q. My son has been taking bipolar medication for ten years and it's not working. He has more outbursts.

A. Medications can cloud our understanding of the illness. There's some indication that the more manias you experience, the more frequently they will come. If the medication is not working as well as before, it may be time for a

change. However, the outbursts may not be a symptom of mania but a side effect because the person is feeling bad and feeling restless. Coming off any medication can be a bad experience, and if the person is not taking his medication regularly, that can be bad, too.

Q. What can you tell us about Klonopin (clonazepam)?

A. It's a benzodiazepine, of the same family as Xanax (alprazolam), Valium (diazepam), and Librium (chlordiazepoxide). It works for anxiety and makes most people calm. It can be given on a schedule or as needed. But Klonopin does have a risk of tolerance, which means you need more of it over time. Ativan (lorazepam) is similar, but the difference is how long it works. Both medications work on the neurotransmitter gamma-aminobutyric acid (GABA) receptor. These drugs are highly addictive and have a potential for abuse.

Q. I've heard Clozaril works when others don't. How long should you wait for them to have effect before you go to Clozaril.

A. Clozaril is one of the newer antipsychotics, and it's been reported that some people with schizophrenia respond better to it than to other antipsychotics. But using it can wipe out blood cells, in addition to causing weight gain and diabetes. It's recommended to try Zyprexa, Risperdal, Seroquel, Abilify, and Gedon first before resorting to Clozaril. You usually need to try each for several months at a time to adjust the dosing, so it can be several years before you want to consider Clozaril.

Q. What's the view of the APA on using drug cocktails instead of single medications?

A. Opinions are all over the map, and prescribing cocktails is quite common. The thought is that you use multiple medications to treat multiple symptoms. But there's not much clinical evidence for using cocktails, because most studies are of one drug against a placebo for one indication. However, if you are taking one medication and are getting better but are still sick, do you change medications or add another one? The latter is usually what happens.

We do have studies on how the body breaks down and gets rid of different compounds. Which enzymes affect the drug is part of the reporting on clinical trials. So it's possible when giving multiple medications to look them up on a table and avoid some of the complications.

Q. Why is it easier to get medications approved in Europe than in the U.S.?

A. Europe in general has different regulations and a faster approval process. But different countries have their rules. For example, the UK restricts antidepressants for adolescents because of the risk of suicide.

Q. What are the long-term side effects of these medications?

A. We're still learning. For example, we've just learned that long-term use of antidepressants is related to loss of bone density. Prozac (fluoxetine) was in general use for a couple of decades before anyone thought to study bone loss. Many of these medications are newer and we're still learning all of the effects.