SPEAKER NOTES

Overview of Psychiatric Medications

Summarized by Thomas T. Thomas

The speaker at our July 22 meeting, **Margo Pumar, MD,** is a Psychiatric Consultant through Alameda County Behavioral Health Care Service's Primary Care/Psychiatry Consultation Program. She has a truly interesting background, having worked in Africa as a clinical educator. As an associate professor with the University of Pennsylvania, Department of Psychiatry, she set up a psychiatry department and medical school course in Botswana in conjunction with the University of Botswana School of Medicine. Dr. Pumar has also worked in Emergency Room psychiatry, psychosomatic medicine, and outpatient psychiatry. She completed her training in the Bronx, New York, at the Montefiore Medical Center of the Albert Einstein College of Medicine and at the UC Davis Medical School.

MARGO PUMAR, MD

Dr. Pumar originally planned a career in cardio-thoracic surgery, but she found she didn't like standing up for hours on end during an operation. Early on, she transferred to psychiatry—which does have a certain stigma in the medical profession. However, her first patient was a woman with schizoaffective disorder. "I was amazed at her strength," Dr. Pumar said. "I love these patients."

A psychiatrist has a lot of tools, she said, and one of them is medications. But it's important to understand that "medications are not like surgical knives. They're not precise. They are hammers."

Most psychotropic medications act on the chemicals that transmit nerve impulses in the brain. "The brain is filled with wires," she said. "And the place where the wire from one cell stops and connects with another is called the 'synaptic cleft.' Neurotransmitters communicate back and forth across this cleft. Medications can increase transmission, or shut down transmission, or attenuate the chemical receptors."

Dr. Pumar described the basic neurotransmitters that these medications affect:

- **Serotonin** governs a person's well being, moods, appetites, memory and sleep. It is also implicated in obsessions and compulsions.
- **Dopamine** governs the brain's motivations, its reward mechanism, and attention.
- **Norepinephrine** affects alertness, concentration, energy, and is part of the "fight or flight" response.
- **Glutamate** is an on-off switch required by neurons for normal functioning.

"All of these neurotransmitters work together to affect a person's mood and cognitive function," Dr. Pumar said. Their actions and the effects they have on

various mental health conditions tend to overlap. And so the medications used to treat those conditions also tend to overlap.

Medications that increase the brain's **serotonin** levels include the "selective serotonin reuptake inhibitors," or SSRIs, which prevent the synaptic cleft from removing excess amounts of the neurotransmitter. These medications include Lexapro, Celexa, Zoloft, Prozac, Luvox, and Paxil. They are generally well tolerated, can affect sleep and energy patterns, initially may cause gastro-intestinal distress, and may cause sexual side effects, tremors, some weight gain (especially Paxil), and some effects on the heart and the body's electrolytes. These medications generally take time to affect mental conditions.

Serotonin-**norepinephrine** reuptake inhibitors, or SNRIs, operate in similar fashion and include Effexor, Cymbalta, and the tricyclic antidepressants. Their side effects are similar to SSRIs but may also include blood pressure changes and anticholinergic side effects such as constipation and dizziness.

Antidepressants are generally used for major depression and related disorders and for anxiety disorders such as generalized anxiety, panic attacks, post-traumatic stress disorder, social anxiety, obsessive-compulsive disorder, and hair pulling. Dr. Pumar noted that anxiety disorders affect 13% of the population and are generally "comorbid" with—or seen in the presence of—one or more mental health or medical disorders.

Antidepressants may also be used for bipolar disorder in association with a mood stabilizer or antipsychotic, in schizophrenia with an antipsychotic, in attention deficit hyperactivity disorder, and in eating disorders, for chronic pain, and for smoking cessation and hot flashes.

One of the first antidepressants to be developed, monoamine oxidase inhibitors (MAOIs), works by blocking an enzyme that removes serotonin, norepinephrine, and dopamine. Because this class of medication can cause high blood pressure and cardiac effects when taken with certain foods, they require dietary restrictions. MAOIs have generally been replaced by the newer antidepressants.

Medications that address **dopamine** include the first generation, or "typical," antipsychotics such as Haldol, Trilafon, and Prolixin, and the second generation, or "atypical," antipsychotics such as Risperdal, Abilify, Seroquel, Zyprexa, Geodon, Latuda, and Clozapine. The first generation medications block the dopamine, or D2, receptors in the brain's cortical pathway, which connects with the cerebral cortex and frontal lobes and governs normal cognitive function, as well as with the nigrostriatal pathway, which connects the parts of the brain governing movement.

Antipsychotic medications are used to treat psychosis—impaired thinking and emotions—which may be associated with schizophrenia and schizoaffective disorder (combining schizophrenic symptoms with bipolar disorder), acute mania, or induced by substance abuse, as well as aggression and agitation.

Too much dopamine causes the negative symptoms of schizophrenia such as apathy, diminished expressiveness, and diminished response to pleasurable stimuli. Too little dopamine—which can result from too potent a dose and excessive D2 blocking—causes the extrapyramidal symptoms (EPS) associated with movement disorders, such as akathesia or the inability to sit still, Parkinsonian-type tremors

and rigidity, dystonias or disturbing and involuntary contractions of major muscle groups, and tardive dyskinesia (TD) or fine wormlike movements, lip smacking, and grimacing. Akathesia tends to go away when medication stops, while tardive dyskinesia happens late in treatment and does not reverse. However, TD seems to be less subjectively uncomfortable for patients than other movement symptoms.

Dopamine also works in the brain pathway that suppresses production of the enzyme prolactin, which controls lactation. If dopamine is blocked, the body produces more prolactin, which can result in sexual dysfunction, breast enlargement, disruption of the menstrual cycle, and lactation in both men and women.

The second generation antipsychotics also block the D2 receptors but also block serotonin 5HT2 receptors. They have fewer extrapyramidal side effects but most have major metabolic side effects. These include increased appetite, which can lead to weight gain, increased triglyceride and cholesterol levels, insulin resistance, and diabetes. These medications can also increase prolactin levels, lower blood pressure, create some cardiac issues, and cause some EPS and TD symptoms—but at lower rates than the first generation.

Addiction is also associated with the dopamine pathways, since this neurotransmitter is involved with the brain's pleasure and reward centers. A medication useful in treating nicotine addiction is Wellbutrin.

Another class of medications are mood stabilizers, which are used to manage bipolar disorder and schizoaffective disorder, usually in combination with other drugs. These medications can include anticonvulsants like Depakote, Tegretol, and Lamictal, as well as both first and second generation antipsychotics. Dr. Pumar noted that medications used to stabilize a patient in crisis are not always right for maintaining that patient in the long run.

One of the longest used and most widely prescribed mood stabilizers is lithium, which treats acute and maintenance manic and depressive episodes of bipolar disorder—although the antidepressive effect takes much longer than the anti-manic effect. This medication has a narrow window between not working at all and causing toxicity, including kidney damage and cardiac arrhythmia, so regular blood monitoring is required. Drugs processed by the kidneys, such as NSAID painkillers, can increase lithium's toxic levels. Evidence shows, however, that lithium does greatly reduce the risk of suicide.

Finally, two medications—Lyrica and Neurontin—which are sometimes prescribed for anxiety, as well as for various nerve-related pain and the onset of seizures, may be involved in mediating **glutamate** in the brain. However, their exact mechanism of action is not clear.

In prescribing any of these psychotropic medications, Dr. Pumar said, she looks not so much at their effectiveness as their safety and side effects. As a general rule for antidepressants, she starts a patient on one-quarter of the standard dose. If after a week the patient seems to be tolerating it, then she will increase the dosage to find the effective range.