

# New Medications for Treatment of Schizophrenia

*Summarized by Thomas T. Thomas*

**Dr. Sophia Vinogradov** spoke to our members on November 17. She is a physician and assistant professor in residence at the University of California and with the Veterans Administration Hospital. Her topic was some of the new medications becoming available in the treatment of schizophrenia.

“We are at the threshold of a whole new era for treatment of chronic mental illness,” she said. “In five to ten years we will look back on the currently available medications and think of them as barbaric.” She particularly noted their side effects and their lack of consistent effectiveness.

As background to her presentation, Dr. Vinogradov explained some recent changes in thinking on this disease. “It’s becoming clear that schizophrenia is a syndrome with many subgroups and causative agents,” she said.

She likened schizophrenia to a fever condition. A century and more ago, physicians thought all fevers were one illness and tried to treat them all the same way. Today, doctors know that fevers arise from different ailments and need different treatments.

The medical community now divides schizophrenia into three broad subgroups:

- **Paranoid schizophrenia**—characterized by paranoia, hallucinations, and delusions.
- **Disorganized schizophrenia**—in which the patient’s thinking, speech, and other cognitive functions deteriorate.
- **Undifferentiated schizophrenia**—with conditions that don’t fit clearly into either of the above categories.

The doctor explained that longitudinal studies have shown several generalities about these subtypes, although she emphasized that not every patient fits into these patterns.

Paranoid schizophrenia is often characterized by an onset that comes later in life and is both sudden and acute. The outcome of treatment is usually better than with other categories, and the patient usually has less problem maintaining hobbies and other interests.

Disorganized schizophrenia generally also has an acute onset. Once started, the course of the disease is severe, and it’s harder for the patient to recover normal functioning.

Undifferentiated schizophrenia has an earlier, more gradual onset; the patient slowly worsens. The condition is chronic and tends not to go into remission.

Dr. Vinogradov then discussed two broad categories of schizophrenic symptoms: positive and negative. Positive symptoms include delusions, hallu-

inations, paranoia—those generally associated with paranoid schizophrenia. Negative symptoms include withdrawal and isolation, lack of social contact, and deteriorated thinking processes—associated with disorganized schizophrenia.

Patients with positive symptoms usually—in perhaps sixty percent of cases—respond well to the currently available medications, the doctor said. However, these drugs work less well with negative symptoms and sometimes even worsen the condition.

At this point Dr. Vinogradov showed a series of slides with computer imaging of human brains, from both schizophrenia sufferers and a control group without the illness. The slides showed structural, metabolic, and cellular differences between the two sets of brains. Clearly then, schizophrenia reflects a physical problem with the brain and its functions, which implies that medication will have an effect on the course of the disease.

The doctor introduced the “Dopamine Hypothesis.” This says that the nerve cells of a schizophrenia sufferer have too many receptors for dopamine, which is a neurotransmitter—one of the class of chemicals which pass between nerve cells, initiating and regulating brain activity.

Support for this hypothesis comes from the fact that street drugs like cocaine are known to enhance dopamine transmission and retention. They can induce a psychosis similar to that experienced in schizophrenia. Because of this hypothesis, many of the current medications used in treating schizophrenia are dopamine blockers. That is, they inhibit the reception of dopamine in the nerve cells.

One trouble with these drugs, however, is that they inhibit reception throughout the brain, and the brain has two major “dopamine tracks.” The first is the limbic system, which governs emotions, perceptions, and some kinds of memory. Here is where the psychoses of schizophrenia seem to originate and where the dopamine blockers operate effectively.

The second dopamine track is the basal ganglia, which coordinates smoothness of bodily movement. The blockers tend to inhibit transmission here as well; the patient then suffers side effects like stiffness, drooling, and involuntary or inappropriate muscle movement.

The new categories of drugs which are now becoming available to treat schizophrenia overcome these side effects in several ways. Some are tailored to operate regionally, on the limbic system but not the basal ganglia. Others work only on certain kinds of brain receptors. Still a third class is designed to work on dopamine in combination with the other neurotransmitters—serotonin and norepinephrine (also called noradrenaline)—to produce more subtle effects.

The names of these various drugs to watch for in coming months and years are Risperidone (which may be commercially available this winter), Remoxipride, Seroquel, Olanzapine, Sertindole, and Zodapine.

Some of these new drugs, unlike the traditional medications, may actually enhance cognitive functions instead of simply shutting down areas of the brain. So they may address schizophrenia’s negative symptoms as well as the positive ones.

None of these drugs, Dr. Vinogradov emphasized, is a cure. They produce remission of symptoms but don’t attack the cause of the illness. Because some of the structural changes in the brain due to schizophrenia seem to take place during

early development, perhaps even in the womb, medication may be unable to reverse the process.

Studies have shown, however, that patients tend to have better outcomes if doctors intervene early and reduce the number of psychotic episodes. That is the promise of these drugs: more effective treatment of symptoms that undermine the patient's outlook and mental functioning.