PASSAGE VIII

This passage provides information on antipsychotic drugs called neuroleptics.

In the 1950s, the development of antipsychotic drugs called neuroleptics radically changed the clinical outlook for patients in mental institutions who had previously been considered hopelessly psychotic. Daily medication controlled delusions and made psychotherapy possible. Many, who otherwise might never have left institutions, returned to society. Now, physicians have learned that there is a price to be paid for these benefits. Approximately 15 percent of patients who undergo long-term treatment with antipsychotic drugs develop a cluster of symptoms called tardive dyskinesia, the most common symptoms of which are involuntary repetitive movement of the tongue, mouth, and face, and sometimes the limbs and trunk.

Neuroleptic drugs interfere with the action of dopamine, an important neurotransmitter in the brain, by binding to the dopamine receptors of nerve cells. Dopamine is a prime suspect in the pathophysiology of schizophrenia. Large doses of drugs such as amphetamines, which stimulate secretion of dopamine, produce a psychosis resembling schizophrenia. Reducing the activity of this neurotransmitter alleviates the delusions that cause 25 percent of psychotic behavior. Although the inhibition of dopamine activity can control psychotic behavior, researchers now believe that the central nervous system of some patients adapts to long-term therapy by increasing the number of specific dopamine binding sites. The net result is dopamine hypersensitivity, which is correlated with the subsequent appearance of tardive dyskinesia.

The risk of developing tardive dyskinesia is not so great that doctors have considered abandoning the use of antipsychotic drugs. Patients generally are bothered only slightly by the physical side effects, though the abnormal movements are troubling and may hinder social adjustment. Additionally, early diagnosis and prompt discontinuation of the neuroleptics might result in a decrease in the incidence of the movement disorders. Unfortunately, without neuroleptic drugs, psychotic behavior returns. So, researchers have tried to achieve a satisfactory balance between the two effects, lowering dosages to a level that minimizes movement disorders yet controls psychosis. In a five-year study of twenty-seven psychiatric patients treated with neuroleptics representing all classes of antipsychotic drugs, researchers attempted to decrease drug doses to their lowest effective levels. Patient responses suggested that low to moderate doses of antipsychotic drugs could control psychoses just as well as high doses, and tardive dyskinesia symptoms stabilized and gradually diminished or completely disappeared.

The fact that psychoses can be controlled at the same time that tardive dyskinesia symptoms are reduced suggests that a drug more specifically affecting the mechanism of psychoses might not cause movement disorders. Sulpiride, a drug not available in the United States but widely used in Europe, where it was developed, may be one such alternative. The drug selectively blocks D–2 dopamine receptors, perhaps especially those in the limbic area of the brain, which is involved in emotion and behavior. It does not adversely affect the adenylate cyclase-linked D–1 dopamine receptors. Sulpiride has proven effective in the short term, but whether it suppresses tardive dyskinesia over a long period of treatment is not yet known.