

Because of these serious side effects, some clinicians believe it is unwise to take high doses of antipsychotics for extended periods of time. Current clinical practice calls for treating patients with the smallest possible doses of drugs. The clinician is put in a bind by this situation: if medication is reduced, the chance of relapse increases; but if medication is continued, serious and untreatable side effects may develop.

**Newer Drug Therapies** In the decades following the introduction of the traditional antipsychotic drugs, there appeared to be little interest in developing new drugs to treat schizophrenia. This situation has changed markedly in recent years, with the introduction of *clozapine* (Clozaril), which can produce therapeutic gains in patients with schizophrenia who do not respond well to traditional antipsychotics (Kane et al., 1988) and has produced greater therapeutic gains in reducing positive symptoms than traditional antipsychotics (Rosenheck et al., 1999; Wahlbeck et al., 1999). Patients who take clozapine are also less likely to drop out of treatment (Kane et al., 2001). In addition, Clozapine produces fewer motor side effects than do traditional antipsychotics. Furthermore, maintenance of discharged patients on clozapine reduces relapse rates (Conley et al., 1999). Although the precise biochemical mechanism of the therapeutic effects of clozapine is not yet known, we do know that it has a major impact on serotonin receptors.

Clozapine does have serious side effects, however. It can impair the functioning of the immune system in a small percentage of patients (about 1 percent) by lowering numbers of white blood cells, making patients vulnerable to infection and even death. For this reason, patients taking clozapine have to be carefully monitored. It also can produce seizures and other side effects, such as dizziness, fatigue, drooling, and weight gain (Meltzer, Cola, & Way, 1993).

The success of clozapine stimulated drug companies to begin a more earnest search for other drugs that might be more effective than traditional antipsychotics. Two results of this search are *olanzapine* (Zyprexa) and *risperidone* (Risperdal). Both have the advantage of producing fewer motor side effects than traditional antipsychotics; perhaps, because of the reduced rate of side effects, patients are somewhat less likely to discontinue treatment (Dolder et al., 2002). The newer drugs appear to be as effective as traditional antipsychotics in reducing positive symptoms (Conley & Mahmoud, 2001), perhaps even better (Sanger et al., 1999). They also appear to be superior to traditional drugs in reducing rehospitalization rates (Csernansky et al., 2002).

A psychological approach to the study of risperidone examines fundamental aspects of cognition, such as attention and memory, that are known to be deficient in many patients with schizophrenia (e.g., Green, 1993) and are associated with poor social adaptation (Green, 1996). Evidence is emerging that risperidone improves short-term memory—involved in, for example, remembering a phone number long enough to be able to dial it—more than other antipsychotic drugs, apparently by reducing the activity of serotonin-sensitive receptors in the frontal cortex (Green et al., 1997). Research has also shown that improvements in memory are correlated with improvements in learning social skills in psychosocial rehabilitation programs (Green, 1996; Marder et al., 1999). Risperidone may thus make possible more thoroughgoing changes in schizophrenia and its behavioral consequences than do drugs that do not have these cognitive effects.

**Table 11.4 Summary of Major Drugs Used in Treating Schizophrenia**

Drug Category	Generic Name	Trade Name
Phenothiazine	Chlorpromazine	Thorazine
	Fluphenazine decanoate	Prolixin
Butyrophenone	Haloperidol	Haldol
Thioxanthene	Thiothixene	Navane
Tricyclic dibenzodiazepine	Clozapine	Clozaril
Thienbenzodiazepine	Olanzapine	Zyprexa
Benzisoxazole	Risperidone	Risperdal

**Evaluation of Drug Therapies** Antipsychotic drugs are an indispensable part of treatment for schizophrenia and will undoubtedly continue to be an important component. They are surely preferable to the straitjackets formerly used to restrain patients. Furthermore, the recent success of clozapine, olanzapine, and risperidone has stimulated a continued effort to find new and more effective drug therapies for schizophrenia. Many other drugs are currently being evaluated, so that we may be on the verge of a new era in the treatment of schizophrenia. See Table 11.4 for a summary of major drugs used to treat schizophrenia.