



Scene from *One Flew over the Cuckoo's Nest*. The character on whom Jack Nicholson is sitting was lobotomized in the film.

ings by others were less encouraging, and insulin-coma therapy—which presented serious risks to health, including irreversible coma and death—was gradually abandoned. As discussed in Chapter 10, electroconvulsive therapy (ECT) was also used after its development in 1938 by Cerletti and Bini; it, too, proved to be only minimally effective.

In 1935, *Moñiz*, a Portuguese psychiatrist, introduced the **prefrontal lobotomy**, a surgical procedure that destroys the tracts connecting the frontal lobes to lower centers of the brain. His initial reports claimed high rates of success (*Moñiz*, 1936) and for twenty years thereafter thousands of mental patients—not only those diagnosed with schizophrenia—underwent variations of psychosurgery. The procedure was used especially for those whose behavior was violent. Many patients did indeed quiet down and could even be discharged from hospitals. During the 1950s, however, this intervention fell into disrepute for several reasons. After surgery many patients became dull and listless and suffered serious losses in their cognitive capacities—for example, becoming unable to carry on a coherent conversation with another person—which is not surprising given the destruction of parts of their brains believed responsible for thought. The principal reason for its abandonment, however, was the introduction of drugs that seemed to reduce the behavioral and emotional excesses of many patients.

Drug Therapies Without question the most important development in the treatment of schizophrenia was the advent in the 1950s of several medications collectively referred to as **antipsychotic drugs**, also referred to as *neuroleptics* because they produce side effects similar to the symptoms of a neurological disease.

Traditional Antipsychotic Drugs One of the more frequently prescribed antipsychotic drugs, *phenothiazine*, was first produced by a German chemist in the late nineteenth century. Not until the discovery of the antihistamines, which have a phenothiazine nucleus in the 1940s, did phenothiazines receive much attention.

Reaching beyond their use to treat the common cold and asthma, the French surgeon Laborit pioneered the use of antihistamines to reduce surgical shock. He noticed that they made his patients somewhat sleepy and less fearful about the impending operation. Laborit's work encouraged pharmaceutical companies to reexamine antihistamines in light of their tranquilizing effects. Shortly thereafter a French chemist, *Charpentier*, prepared a new phenothiazine derivative, which he called *chlorpromazine*. This drug proved very effective in calming patients with schizophrenia. As already mentioned, phenothiazines derive their therapeutic properties by blocking dopamine receptors in the brain, thus reducing the influence of dopamine on thought, emotion, and behavior.

Chlorpromazine (trade name Thorazine) was first used therapeutically in the United States in 1954 and rapidly became the preferred treatment for schizophrenia. By 1970 more than 85 percent of all patients in state mental hospitals were receiving chlorpromazine or another phenothiazine. Other antipsychotics that have been used for years to treat schizophrenia include the *butyrophenones* (e.g., haloperidol, Haldol) and the *thioxanthenes* (e.g., thiothixene, Navane). Both types seem generally as effective as the phenothiazines and work in similar ways. These classes of drugs can reduce the positive symptoms of schizophrenia but have little or no effect on the negative symptoms.

Although the antipsychotics reduce positive symptoms of schizophrenia so that many patients can be released from the hospital, they are not a cure. Furthermore, about 30 percent of patients with schizophrenia do not respond favorably to the antipsychotics just discussed, although some of these patients may respond to newer antipsychotic drugs (e.g., clozapine), which will be discussed later. Because of the side effects of the whole range of antipsychotic drugs, about half the patients who take them quit after one