

HISTORY OF ANTIPSYCHOTIC DRUG DEVELOPMENT

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1 HISTORICAL PERSPECTIVE

Schizophrenia is a devastating mental illness that affects approximately 1% of the world population. The disease is characterized by disordered thinking and behavior, with an equal prevalence in men and women. The symptoms of psychiatric disorder in patients with schizophrenia can be divided into two types, positive and negative. Positive symptoms include hallucinations, delusions, and thought disorder. Negative symptoms represent the loss of qualities normally present in healthy individuals, including diminished emotion, lack of interest, and depressive signs and symptoms. The course of schizophrenia is variable but is usually recurrent and chronic, often causing severe disability. Prior to 1923 only physical methods of treatment were available for schizophrenia in the United States, and in 1923 psychotherapy was introduced in the United States by a European psychiatrist named Adolph Meyers. Psychotherapy was the mainstay of treatment available to manage schizophrenia until the 1950s when chlorpromazine came into the picture serendipitously. The revelation that pharmacological agents can treat schizophrenia led to the explosive growth of psychopharmacology and transformed the “art” of treating mental illnesses to the “science” of modern psychiatry. Currently, there are several classes of antipsychotic drugs available to psychiatrists to treat schizophrenia. Recent studies have shown that taking antipsychotic medications consistently is crucial and necessary to manage the symptoms and to control the risks of relapse. This chapter reviews the history of anti-

psychotics starting with the birth of typical antipsychotics developed over a half century ago, the current newer safer atypical agents for treatment of schizophrenia, and novel emerging therapies being developed in the new millennium.

2 DEVELOPMENT OF PHARMACOTHERAPY OF SCHIZOPHRENIA

2.1 Birth of (Typical) Antipsychotics

The discovery in the 1950s that chlorpromazine could effectively be used to treat schizophrenia was serendipitous. The drug, 4560 RP, later known as chlorpromazine (CPZ), was synthesized in 1950 by Paul Charpentier, a chemist at Laboratoires Rhône-Poulenc in France. Chlorpromazine is chemically a phenothiazine derivative with the IUPAC name 3-(2-chloro-10H-phenothiazin-10-yl)-N,N-dimethyl-propan-1-amine (Fig. 1).

It was designed and synthesized as a medication to reduce agitation or anxiety in patients before surgery. It was the observational ability and curiosity of a French surgeon Henri Labroit that brought to light the magical powers of chlorpromazine in treating schizophrenia. In 1952, with the help of some skeptical psychiatrist colleagues, Labroit tested chlorpromazine in a 24-year-old man who had mania. The medication made the patient calm for several hours with his eyes shut (although his facial expression still looked rather maniacal). Within 3