This article presents a brief summary of indications provided by research on the genetic and biochemical aspects of schizophrenia.

INTRODUCTION

In spite of considerable progress, the understanding of schizophrenic behavior is far from clear. In fact, more questions have been posed in recent decades than have been answered. Not the least of these is the basic problem of whether there is, indeed, such an entity as schizophrenia or whether the observed behavioral aberrations constitute a collection of assorted disorders with similar symptoms. Opinions have ranged from the radical assertion that the illness is a myth, the behavior being a normal response to a deranged environment to long lists of possible environmental and biological causes underlying a heterogeneous symptomology. Whether or not the etiology of schizophrenia is, at least in part, genetically determined, has been subject of considerable debate.

When Bleuler first coined the term in 1911, he spoke about the “group of schizophrenias” that constituted the disease entity previously described by Kraepelin as dementia praecox. At that time a biological and probably inherited basis of the disorders was accepted but could not be demonstrated. Investigators concentrated on describing the symptomology, course, and pathogenesis in an effort to bring the symptoms under a single denominator.

After Freud demonstrated the importance of interaction with the psychological environment, attention began to shift to psychodynamic, and later psychosocial factors in the etiology of schizophrenia. Biological influence was widely discounted. With the advent of technological advances, the interest in physiological and biochemical research returned. Although there is, as yet, no hard evidence for any single specific biological lesion underlying schizophrenia, there is increasing acceptance of the idea that the disorder seems to arise from an interaction of somatic and psychogenic factors, and that some of the somatic factors appear to have a genetic component.

The search for evidence of underlying genetic lesions in mental illness is complicated by the fact that objective and quantitative measures for diagnostic evaluation are not available and the clinical picture presents a high degree of heterogeneity. Agreement on a diagnosis for index cases becomes the first
problem in any study. Bleuler's original description of classic schizophrenia stressed thought disturbances, flattening of affect, ambivalence, and withdrawal as primary symptoms. They are still so considered, but since they are not always easy to document, and secondary symptoms as well as many other clinical manifestations have complicated the issue, the diagnosis of schizophrenia has become an art, relying heavily on the intuition of individual diagnosticians.

Over the years many attempts have been made to define and categorize schizophrenia either as one entity or as a collection of subtypes. On the basis of clinical description, course, pathogenesis, or relation to organic symptoms, a number of classifications have been constructed. However, they are far from clear-cut and not always comparable to each other. Confusion still exists. Even the distinction between schizophrenia and bipolar affective disorders is blurred, since depression and manic symptoms are found in both. For example, a sharp rise in schizophrenia labeling was noted when phenothiazine therapy for this disorder was introduced, whereas the diagnosis of depression rose when lithium salts became available.

Vagueness of diagnostic labels makes it difficult to show clear-cut results and comparison between various studies is complicated. A number of recent efforts have been directed at setting up more universally acceptable criteria for diagnosis in research. One of these is a 12-point system devised under the auspices of the International Pilot Study of Schizophrenia. Another is a computer-based classification developed for the "Iowa 500 Study" on the epidemiology of mental illness. Based on symptom clusters, these systems view schizophrenia basically as one entity, but recognize the possibility of etiologic heterogeneity. For the purposes of epidemiological genetic studies, a "spectrum concept" in schizophrenic and manic-depressive disorders was established (see below). In spite of progress toward diagnostic uniformity, findings to date are difficult to compare and it may be that some conflicting results are artifacts of diagnostic diversity.

Research is being conducted along many lines of inquiry and a good number of them have a bearing on the elucidation of genetic components. This paper will review direct genetic studies, research on biochemical characteristics, and some etiological hypotheses. All offer clues to the understanding of the genetics of schizophrenic behavior.

GENETIC STUDIES

The fact that relatives of schizophrenic patients are at a greater risk for schizophrenia than others has long been noted. The incidence of the overt disease is less than 1% in the general population, whereas there is a 2-5% incidence among parents of schizophrenics, 6-12% among their siblings, and about 15% among their children. Since monozygotic twins are genetically identical and dizygotic twins share only an average of half their genes, the study of twin pairs can provide useful genetic information. Numerous twin studies have set out to estimate the genetic