One of the main questions related to schizophrenia is, naturally enough, what is it? Such a question may seem obvious, naive, impossible, or any combination of these. And certainly it is a bit demanding to expect that anyone could say what schizophrenia is in 1,000 words. On the other hand, we felt that it was worth the effort. We hope that presenting these brief discussions on "what is schizophrenia" by persons who have worked extensively in the field will allow the reader to note areas of overlap and disagreement as well as variations in emphasis. Although no one may yet be able to provide the definitive answer, at least this collection of informed opinions may help clarify the major questions.

The essays by Joseph Zubin and Arnold M. Ludwig are the fourth in this series. Further collections of these statements will be presented in subsequent issues. Readers' responses and comments are cordially invited.-J.S.S., M.B.B., and S.J.K.

"Of the making of definitions there is no end and too many definitions is a weariness of the flesh" (with apologies to Ecclesiastes)

The series "What is Schizophrenia?" comes at a critical point in the conceptualization of this disorder. Schizophrenia with its various etiological hypotheses resembles Pirandello's "Six Characters in Search of an Author." After moving along unconnected etiological trails, it has reached the crossroads where a choice must be made. Defining its present state would seem superfluous in view of the many definitions already available. Instead, the direction it should take will be discussed. Progress has been made in relation to several aspects of schizophrenia during the last decade:

- Clinical description and diagnosis (Present State Examination, Research Diagnostic Criteria, Schedule for Affective Disorders and Schizophrenia, DSM-III)
- Neuropathology (enlarged brain ventricles)
- Neurophysiology (evoked potentials, pupillography, and smooth pursuit eye movements)
- Psychophysical and behavioral approaches (crossover reaction time, cross-modality reaction time, continuous performance tasks, dichotic listening with distractors, span of apprehension)
- Advances in the investigation of attention through the application of information processing have made considerable headway. Other advances have come largely as a result of the application of newly developed technologies (e.g., computed tomography, positron emission tomography, and cerebral blood flow measures) or the borrowing of technologies from other fields—from experimental psychology (e.g., masking, dichotic listening), from psychometrics (e.g., development of interviewing techniques), and from information processing (e.g., memory retrieval).
- Despite these advances in the increase of knowledge, however, understanding of the schizophrenic disorder has reached a plateau, especially with regard to its etiology. Although there were outstanding contributions in the genetic, biochemical, and environmental approaches during the 1950s and 1960s, there have been no similar breakthroughs during the 1970s. Nevertheless, there is a general ferment in the air, leading many clinicians and researchers to feel a new optimism about this disorder, especially in the wake of the recent long-term longitudinal followup studies in Europe (Bleuler 1978; Ciompi 1980b; Huber et al. 1980). A
new paradigm for schizophrenia is emerging, and this commentary is an attempt to capture its essence. There is a general expectation that while the 1970s was the decade of depression, the 1980s belongs to schizophrenia.

While the etiology of schizophrenia is still elusive, it has not prevented workers from devising "as if" etiologies in the form of scientific models. There are at least seven scientific models preempting the field (Zubin and Steinhauer 1981) ranging from those that regard schizophrenia as primarily biological in origin (genetic, internal environment, neuropsychological) with the environmental factors playing only a minor role, to those which regard it as primarily environmental in origin (ecological, developmental, learning) with the biological factors playing the minor role.

It must be remembered that even for the most advanced biological model, the genetic model, there is still no direct evidence that the inherited genetic make-up of the person who develops one or more episodes of schizophrenia is in any way different from that of those who are not subject to such a hazard. It is only an inference based on the fact that an individual who has a consanguinous relative suffering with schizophrenia has a higher risk of developing an episode, and the risk varies with the degree of consanguinity, though with some inconsistencies. Adoption studies tend to indicate that the milieu of the family of origin of the offspring of schizophrenic parents may be less responsible for the development of an episode than was formerly thought, but not all the other nongenetic influences have been ruled out. It would be a simple solution to accept the genetic model as the most tenable and appeal to the low penetrance of the suspected schizophrenic genotype, estimated at .26 (Zubin and Steinhauer 1981), to explain why not all of them reach phenotypic expression. However, the cogency for accepting the genetic model must wait until the actual allele or alleles responsible for the genotype are discovered.

At the opposite end of the spectrum is the ecological model. The evidence for this model is less generally accepted than for the genetic, primarily because there is no counterpart to the consanguinity factor that provides the major evidence for genetic transmission. Because there is no comparable specificity in the ecological sphere, environmental factors have tended to be denigrated. A potential counterpart to consanguinity may perhaps be found in the social network which nourishes the body social in the way that the vascular network nourishes the body physical. Unlike the vascular network whose characteristic functioning is well known, the social network is only now beginning to be investigated. For example, the size, density, and other features of the social network in the general population are still to be delineated. Already, however, deviant or poorly developed networks have been implicated in schizophrenia (Hammer, Makiesky-Barrow, and Gutwirth 1978), as well as in other physical disorders and in mortality rates. An attempt has recently been made to implicate the social network in the maintenance of schizophrenia if not in the source of its development (Perucci and Targ 1982).

Because none of these contrasted sets of models can be shown to be both necessary and sufficient, one is left with the need for integrating all seven models into some type of a supermodel to include the potential etiological sources.

It is suggested that the superordinate to these models is the vulnerability model, an elaboration of the diathesis-stress model (Rosenthal 1970; Zubin 1976; Zubin and Spring 1977). Briefly stated, it makes the following assumptions which constitute the framework of the model: (1) A schizophrenic episode occurs in a vulnerable individual who is subjected to a stress beyond the individual's homeostatic coping ability. (2) If the social network, ecological niche, and premorbid personality prove to be unable to cushion the impact of the stressor, an episode of longer or shorter duration will ensue. (3) If the stress is dissipated, the episode will end sooner or later with or without treatment, and the vulnerable individual will return in the majority of cases more or less to his premorbid or pre-episode level (unless there are continuing iatrogenic consequences). (4) If this level was adequate, the individual will be regarded as recovered or improved and be returned to the social niche occupied previously. If the pre-episode adjustment was precarious, even though a return to it occurs when the episode ends, the individual will often be considered persistently ill, still in the episode. This outcome is usually regarded as a chronic state or residual deficit state. Thus, the only persistent aspect of schizophrenia is vulnerability to future episodes; the episodes themselves are time limited.

Just what proportion of schizophrenics fall into the paradigm described above is impossible to determine now. But the implications of the three European longitudinal studies are that the proportion of persistently chronic schizophrenics is
small, probably only 5 to 10 percent, and that in the long run the outlook for schizophrenia is now more optimistic than in former decades. The absence of such long-term followup studies in the United States prevents a comparison with the European studies.

If schizophrenia is largely episodic, why do we have so many apparent chronic patients in our clinics and hospitals? Elsewhere (Zubin and Spring 1977; Ciompi 1980a; Spring and Coons 1982) a number of reasons for the apparent prevalence of chronic schizophrenia have been delineated. We have already pointed out that some of the chronic patients are pseudochronic, since even when their episodes terminate, the poor premorbid personalities to which they return prevent the end of their episode from becoming apparent. Although 80 percent of Bleuler's (1978) probands had either one episode (hospitalization) followed by a release, or multiple hospitalizations followed by release, the small proportion of patients who persist in their episodes accumulates over the years and gives the false impression that schizophrenia is largely chronic. Chronicity may be a psychosocial artifact caused by the psychosocial consequences of acute attacks of illness. Most of the negative symptoms that characterize chronicity reflect iatrogenic and ecogenetic influences (hospitalism and institutionalism) that are not limited to schizophrenia but also characterize other incarcerated populations (prisons, understaffed nursing homes). Long-term outcome is not related to family history of the illness and, hence, chronicity is probably due to environmental influence. Chronicity is not associated with psychopathology and diagnosis but is associated with psychosocial factors which tend to maintain the episode (deprivation due to poor social network, ecological niche, and premorbid personality), and there is no evidence for any type of somatic, biochemical, or other organic basis for the chronicity of schizophrenia though there is some evidence for such factors in the etiology of the acute, albeit transient, episodes.

Many research workers tend to regard chronic schizophrenia as a distinct category, different in origin from the acute form. In general, although the patients who are classified as schizophrenic tend to appear to be quite heterogeneous, this heterogeneity does not necessarily dictate independent categories. Perhaps the heterogeneity inheres in the premorbid personalities\(^1\) of the individuals who develop episodes. The resulting disorder, though focally perhaps the same for all, appears different because the premorbid personality determines how the impact of the psychosis will fragment the person's behavior (Zubin 1965). Thus, premorbidly compulsive persons will differ in their phenotype from the noncompulsive.

The implications of this vulnerability hypothesis are: (1) that schizophrenia is not the malignant, persistent, deteriorating condition it was once thought to be, and (2) that the treatment of schizophrenia might be guided by considering the contingencies which elicit the vulnerability, as well as the social sources leading to chronicity, so that strategies may be developed to eliminate or modify the impact of such contingencies.

If we could develop markers that would identify individuals who are vulnerable to schizophrenia (and there are some indications that such markers are potentially on the way), we could by judicious intervention through educational means (even as is done in diabetes, allergic conditions, hypertension, and other physical disorders) prevent the occurrence of even initial episodes and the recurrence of future episodes. Because of the malignant outlook that has developed about the label of schizophrenia, it might be desirable to designate it as the Kraepelin-Bleuler syndrome, and thus perhaps liberate it from the currently malignant labeling effect.

References

Perucci, R., and Targ, D.B. Mental Patients and Social Networks.
successive layers of an onion in an quest for identity to peeling off

Henrik Ibsen compared Peer Gynt's quest for identity to peeling off successive layers of an onion in an attempt to get at the "core"—only to find out that none existed. Will this also prove to be the case for schizophrenia, a disorder which, like Mephistopheles, can assume many guises? This question is particularly relevant since no one supposedly unique clinical feature among Bleuler's fundamental symptoms, Schneider's first rank symptoms, or other criteria is found in all schizophrenics or exclusively in schizophrenics.

Inadequacies in methodology and conceptualization plague research on schizophrenia. How can a "schizophrenia" or specific biochemical abnormality be identified for a disorder without pathognomonic features? In a way, the problem is not too dissimilar from that of hypnosis whereby investigators, seeking to capture the elusive essence of trance have determined that all its presupposed characteristic features can be reproduced through other means, such as high task motivation. Skeptics argue that this attests to the artifactual nature of trance; others simply claim that the "irreducible essence" has yet to be found.

Despite these perplexing issues, I have little doubt that the disorder known as schizophrenia represents a legitimate clinical entity, that there are many common denominators among its subtypes, and that this entity is distinctly different from other psychiatric disorders. This is the case even though no two individuals with this disorder display the exact same manifestations and any given individual, followed over an extended period of time, can display shifting symptom complexes, sometimes changing temporarily from an undifferentiated form to one with predominantly catatonic, manic, or paranoid features. Paradoxically, it is the elusive nature of schizophrenia and its protean manifestations which provide a basic clue to its very essence.

A better understanding of this disorder may be gleaned through insights obtained from research and clinical experience with psychotomimetic drugs, such as LSD. Though the earlier notion that these drugs could produce a "model psychosis" has been long abandoned, and appropriately so, certain remarkable parallels still pertain. As with schizophrenia, there are no pathognomonic biochemical or neurophysiological findings associated with these drug-induced states—or, at least, they are not specifiable by current methodologies. Even with a common etiologic agent—e.g., LSD ingestion—the clinical manifestations within individuals are protean, ranging from various "laevo-rotations" of reality and transcendental states to religious-mystical experiences and frank psychoses. What this indicates is that LSD can produce a highly malleable mental state which can be profoundly influenced by the "mental set" of the individual (e.g., expectations, cultural factors, and psycho-dynamics), and the context (e.g., unstructured setting, therapy, and group) within which it takes place. In fact, in our own work, we demonstrated that the expression of the psychedelic experience could be molded substantially through hypnosis or suggestion. Even with this panoply of manifestations, most of which are nonspecific in nature and none of which cannot be found in other alterations in consciousness produced by other means, it is hard to dispute that they derive from a common source—namely, drug intoxication. In other words, a minute amount of chemical, hardly measurable, can be responsible for a broad spectrum of seemingly
unrelated states. What relevance do these observations have for schizophrenia? Simply put, they provide us with a conceptual framework of accounting for the diversity of clinical manifestations encountered in schizophrenia without having to postulate a plethora of different disorders or subtypes. The unknown biochemical aberrations associated with schizophrenia, as with LSD, probably produce a “plastic” mental condition whose expression can be influenced and molded by a host of variables, such as culture, intelligence, education, psychological and situational factors. The effects may wax or wane over time, they may vary in intensity, and various degrees of adaptation to them may take place. With the concept of a malleable brain state, it then becomes possible to account for the different “schizophrenia spectrum” disorders on a basis other than degree of genetic penetrance or biological vulnerability. Other factors, of a learned or cultural nature, may shape the resultant state. Therefore, it would seem that even if a specific “S-toxin” or abnormality is found in all schizophrenics, there still will be a wide range of cognitive, perceptual, affective, and behavioral manifestations, none of which will prove to be pathognomonic but a constellation of which, on a probabilistic basis, will be considered to be more likely associated with schizophrenia than with other disorders. These manifestations of schizophrenia will bear similarities to other altered states of consciousness in which archaic modes of thought, affective lability, perceptual aberrations, or epiphany experiences also may be noted. Because of wide variations in human expression, attempts to display greater precision in defining the clinical characteristics of schizophrenia, in lieu of general features, may simply be comparable to attempts to categorize smoke. We cannot now say with certainty whether schizophrenia is a unitary disorder with many manifestations or a collection of different disorders with similar symptomatology. However, until different etiologies can be demonstrated for different, stable subtypes, I believe that the law of parsimony should be invoked. The search should be continued for a common etiological (albeit complex) basis which, like LSD, can be associated with a wide variety of manifestations. Most of the important breakthroughs in medicine have been based on this premise. This also seems a fruitful approach to adopt in etiological investigations of schizophrenia.

Arnold M. Ludwig, M.D. E.A. Edwards Professor Department of Psychiatry University of Kentucky College of Medicine Lexington, KY 40536