How to Break the Logjam in Schizophrenia

A Look Beyond Genetics

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Despite recent advances in methodology, research in schizophrenia has reached an impasse. A new thrust for research in the field is proposed, and ways for testing its validity are indicated. The status of schizophrenia research is evaluated from the vantage point of six current scientific models for its etiology: genetic, ecological, developmental, learning theory, internal environmental, and neurophysiological (including neuroanatomical). Integration of these models is proposed based on the assumption that schizophrenic episodes occur in vulnerable individuals who under sufficient stress develop a time-limited episode from which all but a small proportion recover. However, even the recovered remain vulnerable to future episodes. Potential markers for vulnerability and for the beginning and end of episodes are classified according to the six etiological models from which they emanate. Recent research in vulnerability is summarized, and directions for future research are recommended.

The 1940s and 1950s might be viewed as the heroic, if not the golden, era of psychopathology. Techniques were less sophisticated, psychopathologists more sure of themselves, and patients more trusting in those days. Psychosurgery, electroconvulsive therapy, and insulin therapy were popular; diagnosis was in the doldrums and psychotherapy in doubt while psychoanalysis flourished; hospitals were overcrowded, community psychiatry nonexistent, sensitivity training and primal screams unheard of; and schizophrenia was still largely dementia praecox. Each new development was received with open arms and great expectations. Psychoanalysis, projective techniques, somatic treatments, genetics, behavior modification, and drug therapy each was heralded as a panacea for either increasing understanding or improving treatment outcome. Unfortunately, their promise remains unfulfilled.

This heroic era ended about 20 years ago with the conversion of locked custodial hospitals into revolving door hospitals and with the psychopharmacological revolution. In retrospect, it is clear that notable advances have been made, if not in understanding, at least in the methodology for obtaining knowledge. Viewed prospectively, however, psychopathology has reached a plateau. A veritable logjam of data and theories obstructs progress toward increased understanding, and a paradigmatic revolution is needed before the logjam can be broken.

The Status of Schizophrenia Research

A brief view of the current status of research reveals the extent of progress toward both defining schizophrenia and understanding its etiology.

Descriptive Approaches

The greatest progress has occurred in the descriptive area, where a systematic approach finally has been achieved. The semistructured interview yields a solid base for classification, and diagnostic labels have been systematized through the Research Diagnostic Criteria (61) and the American Psychiatric Association's DSM-III (1). Despite their imperfections, these descriptive approaches represent achievements in both psychology and psychiatry.

Classic demonstrations of the usefulness of the semistructured interview have been provided by two international studies. The United States-United Kingdom project on diagnosis (11) demonstrated that the alleged difference between London and New York in the ratio of schizophrenic to affective patients was a function of differences in style of diagnosis rather than in the patients themselves. The World Health Organization Pilot Study of Schizophrenia (73) showed...
that the condition is ubiquitous in all nine cultures in which mental patients were examined.

Systematization of the interview and of the diagnostic process through the biometric approach, despite its advantages, poses a danger of fixing current knowledge and procedures. Despite successful innovations, diagnosis can be left neither to the computer nor to the novice. There is a tendency for these techniques to generate the kind of data for which they originally were calibrated. Good as this is for the improvement of the current scene, surprise and unexpected findings are ruled out by the limitations of the instrument, and new and unpredicted possibilities are unlikely to arise. Diagnostic success is built on 34 centuries of careful phenomenological observations of mental patients by astute clinicians. Such observations must continue if we are to avoid being doomed to stagnation on the computer printouts even as our predecessors stagnated on case histories.

Etiological Models

As shown in Figure 1, there are at least six scientific models for the etiology of schizophrenia (79). They range from the molecular biological type exemplified by the genetic model to the field theory type exemplified by the ecological model. Between these poles, the internal environment and neurophysiological models lean toward the genetic, whereas the learning theory and the developmental models lean toward the ecological.

The genetic model may be the most advanced of the six. It has recovered from the depreciation of the high concordance rates for monozygotic twins claimed by Kallman and his generation of investigators, and has been strengthened by adoption studies begun by Heston (23) in Minnesota and Kety et al. (30) in Denmark. It is generally accepted now that genetics may be a necessary but not a sufficient cause of schizophrenia, although its necessary character is debated even by some geneticists (32).

According to the genetic model, the genotype is transmitted from one generation to the next through a deviant allele in a particular location on a specific chromosome in the monogenetic model, or through a number of deviant alleles in various locations in the polygenic model. Clearly, the person who possesses the genotype for schizophrenia does not always develop the phenotype. The most cogent evidence for the existence of the genotype, even when unexpressed, is found in Fischer's study (15) of the offspring of discordant pairs of monozygotic twins. The rate of schizophrenia in the offspring of the affected members of the pairs was similar to the rate for the offspring of the unaffected members, 9 and 13 per cent, respectively, with the difference not being significant. Thus, even identical twins who did not develop the phenotype for schizophrenia carried the genotype for it and transmitted it.

The ecological model has yet to gain as much general scientific acceptance as the genetic model, but it has elucidated several factors widely accepted as associated with schizophrenia. These include socioeconomic status, physical and social characteristics of the milieu, social network supports, and minority status. An advantage of the genetic over the ecological model is its use of consanguinity to measure the degree of genetic similarity. There is no comparable measure for assessing similarity for ecological niches, and claims that ecological factors are necessary or sufficient causes for schizophrenia have not been pressed as hard as claims for the genetic factors.

The search for the etiology of schizophrenia in individual developmental history has not produced definitive results yet. This is primarily because of its retrospective nature and because of the lack of scientific models for integrating the data. With Piaget's hypothesis of developmental stages for the increasing complexity of cognitive and language behavior, and with the hypotheses for the evolution and patterning of attachment, socialization, and moral behavior and deviations from it by other theorists, crucial contingencies in which normal behavior could develop became demarcated. When these developmental stages become established firmly, they may provide an underlying framework for delineating normality or psychopathology.

While awaiting the scientific establishment of developmental stages, such indicators as prenatal complications, nutritional deprivations, and retarded maturational development may yield measures associated with the subsequent development of schizophrenia. Recently, Kinney and Jacobsen (32) indicated that season of birth (winter) and likelihood of cerebral

![Fig. 1. Scientific models for the etiology of schizophrenia.](image)
injury after birth are found more frequently in probands of low genetic risk (those who have no affected biological parent, sibling, or half-sibling) than in those of high genetic risk (those who have affected relatives). They conclude that at least some of the low genetic risk probands are not genotypic schizophrenics, but environmentally induced phenocopies, thus giving the developmental model and the other nongenetic models considerable etiological support while freeing the genetic model to deal only with genotypes. Again, there is no conclusive evidence as yet that developmental factors are necessary or sufficient etiological agents. Perhaps when the currently popular studies of high risk children come to fruition, a better understanding of the role of development in the etiology of schizophrenia will become possible.

The learning theory model postulates that the etiology of schizophrenia may be found in the reinforcement history of the individual. Adolf Meyer was a progenitor of this hypothesis in stressing the accumulation of faulty habits in reactions to life’s exigencies as the cause of dementia praecox. Ineffectual social and interpersonal relationships, whether developed actively in maladaptive situations or passively through inappropriate modeling, can make individuals more vulnerable to later stresses. According to this model, the family is an important etiological agent in transmitting attitudes, habits, values, and communication patterns. This type of learning model overlaps considerably with the developmental model. A more strict and rigorous version of the learning theory model in psychopathology denies the assumption of underlying disease, disorder, or even diathesis, and postulates instead that disordered behavior must be investigated in terms of the contingency in which it occurs and the effect it produces. This has given rise to the immediacy hypothesis (53) that the immediate stimuli in time and space rather than remote stimuli have a much stronger effect on schizophrenics than on normals, and that this is why schizophrenic behavior appears deviant; yet, there is still no cogent evidence for causality.

The internal environment model has contributed to progress in both biochemistry and psychopathology. The search for peripheral metabolic correlates of schizophrenia that were observable in the blood and urine failed because the findings were nonspecific. The focus of research then shifted to central synaptic mechanisms. As Kety (29) has indicated, a basic change has occurred in our understanding of the synapse. It is regarded no longer as an electrical junction, but as a chemical switch point at which metabolism, hormones, and drugs may affect the psychological processes mediated through the synapses, including perception, cognition, attention, motivation, mood, and other emotional and mental states. Kety concluded, however, that “although...the mechanisms of action of the drugs effective in the treatment of mental disorders are becoming well defined, the metabolic and biochemical factors involved in schizophrenia and the affective disorders have not been elucidated” (29, p. 86).

The neurophysiological model has provided a considerable number of techniques for examining how the schizophrenic's brain functioning affects information processing. Deviations may occur at any level in information processing, from reception of the stimulus, through encoding and processing to higher centers, to interaction with stored memories of previous experiences and established network patterns, and emission of the final response. Among the techniques useful in differentiating schizophrenic from other mental patients and from normals are: reaction time measures such as the crossover index of Rodnick and Shakow (49), the cross-modality effect of Sutton et al. (65), and the redundancy effect of Bellissimo and Steffy (3); and event-related potentials, especially the P300 of Sutton and Tueting (67), the pupillography of Steinhauser et al. (62) and Rubin (51), and the smooth pursuit eye movements of Holzman (25). Thus far, the results are only promising.

The Current Impasse

Interaction between the genetic and ecological models reveals the state of the art in both and can indicate the gaps that need to be filled. It is well known that genetic endowment does not determine an individual's traits (including the disorders he may develop); rather, the genes determine the responses of body and mind to environmental forces. The genetic model ideally requires the presence of specific genes for the disorder to develop, while the ecological model requires the presence of specific environmental agents or of stress produced by a variety of agents. Until now, except for such conditions as those due to inborn errors of metabolism, the genetic basis for mental disorders was inferred from factors such as consanguinity. But despite its advances, the genetic model has not yet been able to account for the approximately 60 per cent of monozygotic twins who are discordant for schizophrenia. Furthermore, in the four-fold table between pairs of identical twins, only three cells usually are filled, as shown in Table 1. These are the cells for the concordant pairs, and the two cells of discordant pairs. The fourth cell, in which the pairs are concordant for the absence of the phenotype, never is mentioned.

Analysis by Robert Golden (personal communication), based on assumptions that permit an estimate of the frequency for the missing cell, indicates that the proportion of unexpressed to expressed genotypes is...
TABLE 1
Concordance for Phenotypic Expression of Schizophrenia in Pairs of Monozygotic Twins

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* Note: ++, concordance for presence of phenotype; --, concordance for absence of phenotype; +, --, discordance for presence of phenotype.

2.8:1.0, that is, for every genotype that achieves phenotype expression, there are nearly three that do not express it. This leads to an expectation of 3 to 6 percent schizotropes\(^3\) in the general population, based on the genetic model alone. If the other models contribute equal proportions of schizotropes, there may be many more in the general population (and hence in control groups) than is realized. In summary, having demonstrated that some individuals are at greater risk for an episode of schizophrenia by virtue of their consanguinity with probands who have developed episodes, the genetic model is unable to advance further toward locating the allele or alleles for the disorder, explaining why only a minority of genotypes develop into phenotypes, or linking the DNA activity of the genes with the internal environment. One might even go so far as to postulate, heretically, that genetic endowment may be only a contributing factor. That is, it may be neither necessary nor sufficient of itself to elicit an episode in a schizotrope whose vulnerability may be based on totally different, perhaps environmental, causal factors such as postnatal cerebral trauma or a deviant social network.

The ecological model, despite the variety of etiological agents attributed to it, thus far has not provided cogent evidence for the necessity or sufficiency of these agents. The reason for this may lie in the possibility that the stresses impinging on the ecological niche occupied by an individual may be produced by multiple events and contingencies that have no common denominator other than their stress-producing quality. A survey of the remaining models leads to the same conclusion, that despite notable advances made in each, neither necessary nor sufficient etiological causes for schizophrenia have been found in any of them (82). This is our impasse; how to break this logjam is our immediate problem.

\(^3\) In searching for a term to identify the individual vulnerable to schizophrenia, "schizotype" seemed appropriate, but it has been preempted by Rado and subsequently by Meehl, who have limited its meaning to the personality accompanying the genotype for schizophrenia. Therefore, the term "schizotrope" is used here to designate a person prone to develop schizophrenia, regardless of the special etiotypes on which his vulnerability is based.

Etiotypes

The monopoly that genetics held over the etiology of schizophrenia until recently has been broken by the geneticists themselves. They now admit that phenocopies may exist, that is, that schizophrenia may develop in individuals who do not possess the genotype for schizophrenia (32). Thus, etiotypes may be postulated for the other models as follows: an ecotype for the ecological model, an auxanotype\(^4\) (from the Greek root for growth, auxinein) for the developmental model, a mathetotype\(^5\) for the learning theory model, a chemotype for the internal environment model, and a neurophysiotype for the neuropsychological model. Each etiotype characterizes individuals vulnerable to schizophrenia on the basis of the model from which it is derived.

It should be noted, however, that there is a temporal distinction between the genotype and the other etiotypes. Whereas the genotype presumably is laid down when the ovum is fertilized, the other etiotypes do not germinate until a life experience such as a perinatal problem, long term stress, cultural transmission, or traumas render the individual vulnerable.

One question arising at this point is whether the schizophrenia according to these etiotypes is the same disorder, or whether each model describes a different disorder. Until proved otherwise, it will be assumed that the behavior pattern or patterns designated as schizophrenia are equivalent, even though the paths leading to them may be heterogeneous. This follows the assumption underlying the etiology of cancer: types of cancers are classified not by the carcinogens that seem to give rise to them, but by the type of cancerous development incited. Although many paths may lead to a schizophrenic episode, we will assume for the present that they all culminate in the same type of disorder, i.e., that there is a common syndrome to schizophrenia. Thus, it is assumed that there is a congeries of behaviors characteristic of schizophrenia and consisting of many components not all of which need be present when an episode develops, i.e., schizophrenia is a polythetic rather than a monothetic category, to use Sneath and Sokal's phrase (59).

Another question concerns the manner in which the etiotypes bring about their effects. Since the gene itself consists of DNA that transmits its information via RNA messages as protein products, it is not impossible to conceive how genetic factors, interacting with the biochemistry of the internal environmental model and the neuropsychological model, produce imbalances in substances such as dopamine. Similarly, it is not dif-

\(^4\) Suggested by E. I. Burdock.
\(^5\) Suggested by Kurt Salzinger.
ficult to imagine how non-genetic components of the chemotype and neurophysiotype bring about their effects. It is still a mystery how external stresses produce their effects, especially in the ecotypes, aux-anotypes, and mathetotyopes, in which stress-producing situations, such as low socioeconomic status, death of the mother before the subject reaches age 11, or absence of intimacy in adolescent friendships, must be encoded into the internal environment or neurophysiological substrate of behavior to produce vulnerability. Furthermore, if exogenous life events are needed to trigger the various etiotypes, how is this accomplished? The mechanism whereby these external events interact with the central nervous system is still unknown (72).

The Vulnerability Model

Thus, although all of the models aim at a common goal, there has been little or no communication among them until recently. Since none of the models is claimed to be a sufficient cause in the etiology of schizophrenia, it may be postulated that the interaction among them is the essential factor in the development of an episode. The vulnerability model is a superordinate model that integrates the contributions of each of the others and provides for their interaction. The vulnerable individual, the schizotrope, may possess any one of the etiotypes discussed above, or any combination of them. Thus, although no single etiotype is in itself a necessary and sufficient etiological agent, the interaction among them can produce a schizotrope. Such an individual, vulnerable as he is, may never develop an episode, or, under suitable circumstances, may develop one or more episodes. The dimensions of the vulnerability model are: a) degree of vulnerability; b) life event stressors required to trigger or actualize vulnerability; and c) moderating variables such as social networks, premorbid personality with regard to competence and coping, and the physical, social, and cultural parameters of the ecological niche.

Degree of Vulnerability

The vulnerability dimension represents the risk of developing an episode. Corresponding to the two ends of the spectrum for the six models—the genetic and the ecological—there are two types of vulnerability. Inborn vulnerability encompasses elements from the genetic, neurophysiological, and internal environmental models. Acquired vulnerability represents the influence of prior experience (the ecological, developmental, and learning theory models): exposure to traumas, specific diseases, or other early life events such as perinatal complications; family interactions; lack of intimacy in early adolescent friendships. Whether vulner-

nerability extends to all people or only to a select portion of mankind is open to question. The degree of vulnerability in an individual emerges from the concept of health as the maintenance of a dynamic equilibrium against insults continually emanating from the chemical, physical, infectious, psychological, and social environment (2). When this equilibrium is disturbed beyond its capacity to reinstate its own homeostasis, a disorder ensues. Clearly, the same disturbing event may produce a disorder in one person but not in another, depending upon individual differences in resistance to the event, or in vulnerability, and in the moderating variables of social networks, premorbid personality, and character of the ecological niche.

The vulnerability model differs from that developed by Falconer (14) for a more general disease situation. By combining genetic and environmental causes of disease, including the triggering elements, he developed a liability factor that he regards as normally distributed in the population and that must reach a certain threshold before an episode will develop. In both models the vulnerability factor contains both hereditary and environmental contributions. In the vulnerability model, however, challenging life events are separated from the vulnerability factor to delineate the boundary or threshold level that the stressor must transcend before an episode can develop (see Figure 2).

Triggering Events

To elicit an episode in a schizotrope, a triggering event is needed. Such an event is defined as one that

![Figure 2: Relation between vulnerability and challenging events. (The equation for this hypothetical curve is \( V = K \), where \( V \) is the degree of vulnerability, \( S \) is the degree of stress induced by the challenging event, and \( K \) is a constant (77).)]
elicits a crisis in a vulnerable individual. The triggering event is distinguished from a precipitating event, defined by some researchers (7) as one that brings on an episode that in any case would have occurred sooner or later. In contrast, the vulnerability model postulates that unless the triggering event occurs, no episode will follow. Furthermore, the triggering event necessary to elicit an episode is not to be confused with etiological life events giving rise to the various etiotypes (ecological, developmental, learning). These are long term influences that induce vulnerability. Triggering events, in comparison, are short term recent inducers of sufficient stress to produce a crisis. They are undesirable, novel, unexpected, unanticipated, and uncontrollable; produce losses; and require considerable readjustment. of daily routine.

There is considerable evidence available on the role that triggering life event stressors play in eliciting both physical and mental disorders (6, 12, 48, 63). If the strain of readjustment is severe enough, the event triggers first a crisis and then, in a vulnerable individual, an episode of illness, as shown in Figure 2.

The impact of the event on the individual’s social network support system may be the common denominator in triggering the crisis and episode. In the life event schedule of the social readjustment rating scale developed by Holmes and Rahe (24), 86 per cent of the items involved disruption in the individual’s established social network (death of spouse, divorce, etc.). The social network serves two functions in the vulnerability model: a) an etiological function as a possible indicator of the ecotype, insofar as a skewed or constricted social network may characterize the schizotrope; and b) a dynamic function as an agent for absorbing or failing to absorb the impact of life event stressors. Thus, certain losses can be withstood by the vulnerable individual so long as the social network exists and remains intact.

This hypothesis can be tested readily by obtaining pre- and postmorbid data about the contacts an individual makes prior to an episode: With whom did he discuss his problem? Whom did he see and how frequently during the year prior to the immediate preepisode period? According to this hypothesis, those who develop an episode should show an alteration of the social network just prior to the episode.

Recent research in life events, using life event schedules in which standard stressfulness weights for the items are applied, has tended to discount the role of life events in triggering episodes of schizophrenia (47). This may challenge the general use of standard schedules that are based on middle-class norms. It is likely that everyday life events, rather than the dramatic life events of the standard schedules, are the important triggers for the schizotropes. Such everyday events as a rebuff from a neighbor hardly affect the nonschizotrope, but may trigger an episode in the schizotrope. It is also possible that some of the triggering events may be endogenous, produced by internal biochemical changes whose exogenous sources, if any, are difficult to trace.

Moderating Variables

The literature on the role of moderating variables in the development of an episode has been discussed elsewhere. Here, it is important to point out that two individuals of equal vulnerability, similarly stressed by a triggering event will not both develop an episode if the moderating variables of social network, personality, and ecological niche differ in their cases. For this reason, it is important to assess these variables premorbidly. There is a definite association between premorbid status with regard to competence and coping and the development of an episode. Similarly, as has been pointed out, social networks play an important role, and the role of physical, social, and cultural aspects of the ecological niche is well documented.

The role of premorbid competence and coping is rather crucial to the vulnerability hypothesis, since one of its tenets is that all episodes are time limited and that the individual returns to his or her premorbid status when the episode ends unless nosocomial or iatrogenic interventions have interfered with the natural course of return. To determine when an episode begins and ends, there must be some way of assessing the individual’s premorbid status in adapting to life exigencies. To avoid circularity and to minimize any influence that the disorder or vulnerability to the disorder may induce, only the premorbid status in competence and coping is included in the model.

The nature of the relationships among premorbid coping, competence, vulnerability, and life event stressors has been described (82), and will be outlined only briefly here. By competence is meant the abilities, skills, and accumulated know-how in solving life problems. Coping refers to the attitudinal, motivational stance of an individual facing an adaptational crisis. Thus, competence represents the basic ability to deal with the exigencies of life, whereas coping refers to the capacity for directing one’s competence in solving life’s exigencies. Coping may vary from insufficient arousal to deal with the problem optimally to overarousal in which the individual no longer can direct the energy into suitable channels.

The Question of Orthogonality

In evaluating the proposed model, one must determine first whether or not the major dimensions—
vulnerability, triggering events, moderating variables, including competence and coping— are orthogonal. It has been suggested that premorbid competence and triggering events may be related because more competent individuals are more involved with the demands of life and, therefore, more likely to be subjected to clear-cut life stresses. In fact, Spring (personal communication) has shown that schizophrenics tend to experience fewer triggering events than their unaffected siblings. Whether this greater tendency in competent premorbid to perceive life stresses will lead to transitory crises or to actual episodes is not clear. Only empirical investigations can answer the question finally. The generally accepted belief that only the premorbidly poor copers and incompetents fill our hospitals and clinics is not well founded, however.

Some evidence for orthogonality in the other dimensions of the model has been presented (82), but the appeal of orthogonality is based primarily on logical parsimony. Therefore, for the structure of the proposed model, it is assumed that the dimensions all are orthogonal. Premorbid competence may be either high or low and, depending upon the degree of vulnerability and the presence of triggering life events, an episode will either develop or not develop. Similarly, premorbid coping ability may be high or low, regardless of competence and vulnerability. Should the data contradict the assumption, it can be dismissed.

The Episodic Nature of Schizophrenia

While affective disorders long have been regarded as episodic, the schizophrenic disorders, despite some evidence to the contrary, have been regarded as persistently chronic. In contrast, the vulnerability model assumes that the only permanent feature in schizophrenia is vulnerability to future episodes but that episodes are time limited, arising in the wake of the triggering life events and abating when the stress and its aftermath dissipate.

Zubin and Spring (82) have summarized the evidence for this assumption. Most telling is that provided by Bleuler (5), who dispelled the myth that schizophrenia condemns the patient to a life of permanent disability and slow degeneration. In his classic study of the lifetime follow-up of 308 admissions to the Burgholzli Hospital he directed, he found that only one quarter of the first admissions were inpatients at any given point in time during the 23-year follow-up and that as many as 30 per cent of those were in the hospital for nosocomial or egocentric rather than psychiatric reasons. The remainder were living in the community and tended to improve with time. When only those first admissions who were stabilized in outcome for a 5-year period were considered, 30 per cent were completely recovered, 38 per cent mildly affected, 17 per cent moderately affected, and only 15 per cent were persistently chronic. Furthermore, these outcome figures were fixed only for the group. Individual patients shifted from one type of outcome to another. This constancy of outcome for the group across time and inconstancy for the individual is a puzzle until we invoke the vulnerability hypothesis. Since it assumes schizophrenia to be episodic, it would be expected that some patients would be emerging from their episodes while others would be entering new episodes at any point in time. If these numbers are approximately equal, the proportions for the total group would remain approximately constant as the individual episodes wax and wane. The puzzle of group constancy and individual inconstancy disappears in keeping with vulnerability expectancies.

Further evidence for the episodic nature of schizophrenia is offered by Wing (74), who reports a good outcome in 75 per cent of the first admissions followed up after 5 years. Even patients with poor prognoses (4), and even those who occupy the back wards of hospitals (44), have shown unexpectedly good outcomes. If all schizophrenics were considered, including the milder outpatients and undetected patients in the community, the outcome might be even more benign, and the proportion of permanently disabled reduced even further. Bleuler (5) points out that the reason why his father’s generation regarded the outcome of schizophrenia as so bleak was that they only saw recidivists who returned to the clinic but never again saw those who recovered completely. It is also possible that schizophrenia itself may have undergone a metamorphosis from a malignant to a more benign condition, as if the agents responsible for it have become less virulent. Similar transformations have occurred in certain contagious disorders, which seemed to decline in severity even before their causes and treatments became known (22, 81). Whether this represents a change in the disorder, in attitudes toward it, or in treatment of it, is moot; on balance it appears that all three—the disorder, the attitudes, and the treatment methods—have changed.

To account for the so-called chronics in schizophrenia, several factors must be considered. First, as Bleuler reports, a small proportion (no greater than 15 per cent) actually may be chronic, although even some of them may be regarded as recoverable or as victims of circumstances other than those associated with the natural history of the disorder. Second, there are many pseudochronics who have adapted to the chronic life even though their episode is long past. Thus, although both good and poor premorbid tend to recover from
episodes and return to premorbid levels, it is often
difficult to recognize recovery in the poor premorbid
because the level of adjustment to which they return
may be attributed mistakenly to the persistence of the
episode.

Types of Markers

To subject the vulnerability model to experimental
verification it is necessary to develop markers that
can identify vulnerable individuals. The search for
markers is conducted in all of the etiological models
described above, although the term “marker” is defined
differently in various disciplines. As used here,
“marker” designates a specific type of performance or
behavior that characterizes individuals who are having
or have had an episode of schizophrenia (80). Ideally,
such behavior should be specific for schizophrenia and
not characteristic of nonschizophrenics. To establish
the validity of a marker, one must begin with individ-
uals who already have exhibited their vulnerability by
suffering from one or more episodes of schizophrenia.
Once the marker is established as an index of vulner-
ability, it can be used to identify those who, although
they have never had an episode, nevertheless carry
the marker indicating susceptibility.

Efforts are underway to isolate vulnerability markers,
however, at present most of this work deals with
patients during an episode. Hence, it is difficult
to determine without further follow-up whether a
given indicator is a vulnerability or an episode marker.
To differentiate between episode and vulnerability
markers, the character and status of the marker must
be known before, during, and after the episode. The
sequential relationship of types of markers by pre-
episode, episode, and postepisode status is shown in
Table 2.

Four types of markers are indicated in the table: a)
vulnerability markers that persist after the episode, A
and C; b) episode markers that wax and wane with the
episode, B; c) residual markers that appear in the
wake of the episode, E and G; and d) normalization

markers that are present prior to the episode but
disappear when the episode ends, D and F.

In Table 2, then, A is a potential vulnerability
marker since it characterizes the person before, during,
and after the episode. B is an episode marker since it
is present during the episode but not during the pre-
episode or postepisode periods. C is a vulnerability
marker that normalizes during the episode. An exam-
ple of such normalization is the level of homovanillic
acid during the acute stage of schizophrenia (45). D
reflects the normalization of the indicator as a result
of the episode, the marker disappearing in the post-
episode period. E shows the residual effect of the epi-
isode, since the marker was absent in the pre-episode,
but developed in the postepisode period. F indicates
that the episode normalized the marker, causing it to
disappear in the postepisode period. Marker G, like E,
shows the residual effect of the episode, while H is a
nondifferential marker for schizophrenia.

Sibling Concordance

Another way of determining the character of the
marker is to examine the siblings of the probands.
Since siblings on average have 50 per cent of their
genetic makeup in common and also share a common
environment, an investigation of siblings might clarify
the nature of the markers, especially whether they are
vulnerability or episode related. Table 3 uses the types
of markers developed above to show the variety of

<table>
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<td>+</td>
<td>Vulnerability, normalized by episode</td>
</tr>
<tr>
<td>DD</td>
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<td>+</td>
<td>Vulnerability (nonfamilial),</td>
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<td>normalized by episode</td>
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<td>Residual effect of episode</td>
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<td>EE</td>
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<td>F</td>
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<td>FF</td>
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<td>Vulnerability (nonfamilial),</td>
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<td>normalized by episode</td>
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<td>-</td>
<td>+</td>
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<td>Residual effect of episode</td>
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<tr>
<td>GG</td>
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<td>?</td>
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<tr>
<td>H</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>Nondifferential for schizophrenia</td>
</tr>
</tbody>
</table>

* Note: +, marker present; −, marker absent; ?, uncertainty
whether pattern occurs in nature.
possibilities when the status of the siblings is considered. Nonfamilial markers and patterns of uncertain validity are indicated with double letters. A nonfamilial marker designates a characteristic that developed as a result of certain individual experiences not shared by all family members. It certainly would not characterize the genotype but might characterize the other etiotypes. A plus sign (+) appears in the column under sibling to indicate that the marker has a statistically significant higher frequency of occurring in siblings of probands than in control siblings in the general population. A minus sign (−) indicates that the frequency of the marker in siblings of probands is no greater than in the control group.

Marker A in Table 3 remains a vulnerability marker and its character is confirmed by its presence in the sibling. AA is apparently a permanent characteristic of the proband but not of the sibling and hence might be a nonfamilial marker. B remains an episode marker, although BB is not easy to explain and may be an impossible pattern. C and CC are vulnerability indicators that normalize during the episode, C being more likely a familial marker, while CC is probably nonfamilial. D is definitely a vulnerability marker that disappears during and after the episode, so that siblings who develop an episode also would be expected to lose the marker. DD also shows the normalizing effect of the episode. E represents a residual aftereffect of the episode. EE is absent during the pre-episode period but present during and after the episode as well as in the sibling. Only a follow-up of the siblings to see if they develop an episode can reveal the significance of this type of marker. It also is possible that this pattern will not appear in nature. F represents a marker for vulnerability that disappears in the proband after the episode ends, but that may have a familial basis, since the sibling exhibits the marker. A follow-up of the sibling may indicate that if he develops an episode he too may lose the marker. FF is similarly a vulnerability marker that normalizes during the postepisode period but is possibly a nonfamilial vulnerability marker since the sibling does not exhibit it. G shows the residual effect of the episode. GG is perplexing, since it seems to appear only after the episode, and its presence in the sibling is a puzzle. Only a follow-up of the siblings who show the marker will reveal its true nature. H is nondifferential for schizophrenia, and HH can be examined only by a follow-up of the siblings.

**Episode Prediction**

Even with an understanding of the types of vulnerability and episode markers and an awareness of stress-producing events that can trigger crises and episodes, predicting episodes and their outcome remains uncertain. It is important for this purpose to distinguish between indicators that predict the probable occurrence of an episode—prognostic factors—and those that only mark an individual as vulnerable, regardless of whether he ever develops an episode. Even for monozygotic twins, for example, the probability of the second member of the pair being affected if the first member develops an episode is less than 50:50.

The only possible generalization in this respect follows on the well known principle that the past is the best predictor of the future, i.e., those who have had previous episodes are at greater risk for future episodes. Predicting the initial episode is moot, since it involves the three independent factors of vulnerability, exposure to a sufficiently stressful triggering event, and the three moderating variables. Predicting the recurrence of an episode, ordinarily referred to as a relapse, means recognizing that relapses can be of two kinds: a) exacerbation of an ongoing episode; and b) occurrence of a new episode. The ecological niche to which the patient is returned, especially its emotional atmosphere (38), is crucial here. If the patient is not fully recovered from an episode, an early return to the deleterious niche will exacerbate the ongoing episode or, eventually, elicit a new episode.

The past also is the best predictor of the outcome of episodes. It generally is accepted that good premorbid personality leads to good outcome and poor premorbid personality to poor outcome; but this is to be expected on the basis of the vulnerability model, since one of its assumptions is that all episodes end and return the patient to his premorbid status. If premorbid adjustment was adequate, his return to it may be regarded as improvement or even as cure. However, return to a tenuous premorbid adjustment will not be recognized as an improvement, and the patient may be regarded mistakenly as still in the episode. That is why some poor premorbid are regarded as still unimproved even though the episode is long past, and why treatment sometimes is continued unnecessarily to the point of such side effects as tardive dyskinesia. This indicates the need to develop objective episode markers independently of the clinician’s judgment.

**Potential Vulnerability Markers**

The markers that characterize individuals prone to episodes of schizophrenia can be classified according to the etiological model from which they spring. Potential vulnerability markers are listed by etiotype in Table 4.

**Genotype Markers**

Consanguinity with a schizophrenic patient is the only potential indicator or marker now available for predicting the episode.
<table>
<thead>
<tr>
<th>Model Type</th>
<th>Etiotype</th>
<th>Potential Vulnerability Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic</td>
<td>Genotype</td>
<td>Consanguinity, HLA (human leukocyte antigen) typing</td>
</tr>
<tr>
<td>Ecological</td>
<td>Ecotype</td>
<td>Migration, social marginality, socioeconomic status, social isolation, emotional milieu of home, deviant social network</td>
</tr>
<tr>
<td>Developmental</td>
<td>Auxanotye</td>
<td>Season of birth (winter), postnatal cerebral damage, ophthalmologic defects in probands and relatives, absence of intimacy in adolescence</td>
</tr>
<tr>
<td>Learning theory</td>
<td>Mathetype</td>
<td>Severe communication disorder, inability to develop adaptive behavior or benefit from past experience, inappropriate reinforcement</td>
</tr>
<tr>
<td>Internal environmental</td>
<td>Chemotype</td>
<td>Levels of monoamine oxidase, dopamine-beta-hydroxylase, red blood cell catechol-O-methyl transferase, serum creatinine phosphokinase, platelet monoamine oxidase activity</td>
</tr>
<tr>
<td>Neurophysiological</td>
<td>Neurophysiotype</td>
<td>Pupillary response, smooth pursuit eye movements, reaction time crossover index</td>
</tr>
<tr>
<td>Neuroanatomical</td>
<td>Neuroanatomotype</td>
<td>Dilated ventricles, muscle anomalies, cerebral blood flow anomalies</td>
</tr>
</tbody>
</table>

Identifying the genotype. Only in a pair of discordant identical twins is there certainty that even the unaffected member is a genotype. For other blood relatives of schizophrenics, the probability of being a genotype varies with the degree of relationship. Recently, human leukocyte antigen (HLA) typing has been reported to be associated with the presence of schizophrenia (10, 13, 56, 58, 69). Most of the proposed biological markers are still quite controversial, and none has claimed to be pathognomonic for schizophrenia. Because of their controversial nature and since their genetic basis has not yet been established, they are listed below, under potential chemotypes.

**Ecotype Markers**

Markers arising from the ecological model are either physical or social parameters of the ecological niche. Physical parameters include the type of housing, neighborhood, and other characteristics of the niche the individual occupies, whereas social parameters refer to the atmosphere of the household, family relationships, friends, and social networks. In order to integrate the ecological factors, they may be classified, as suggested by Hammer et al. (20), according to the individual’s social network and the degree of support, constraint, or freedom imposed on it by the ecological niche. In classifying social networks, it is important to separate their structural aspects (density, interconnectedness, branching) from the quality of an individual’s participation in the network. The formal characteristics of the network generally seem less influenced by the individual’s personality than the qualitative aspects of the network, but the relationships that make up the social network comprise the basic and universal building blocks of social structure. Analysis of their formation, maintenance, and severance may provide insight into the relationship of social factors to psychiatric disorders. For example, the poor physical facilities in a ghetto niche may restrain the size and intimacy of the network, discourage network development, or disrupt the network through violence, bereavement, or forced relocation.

The role of the social network in moderating the impact of triggering events that lead to an episode in a vulnerable person has been discussed. Is there evidence that social networks are important in characterizing the schizotrope? The presumptive evidence comes from reports that migration, social marginality, and lack of acculturation (all associated with higher rates of schizophrenia) also disrupt or constrain the social network. Social class, which correlates negatively with the rate of schizophrenia, is also a factor in the social network breakdown, since there is a high risk of disruption in the social network at lower socioeconomic levels (higher mortality, forced moving, relocation stress, social isolation, migration). The empirical evidence comes from reports that schizophrenics tend to have smaller networks and that those who, in addition, have networks with low levels of interconnectedness run a higher risk of rehospitalization (43, 60, 68).

**Auxanotype Markers**

One possible systematic approach to detecting vulnerability markers related to maturation and development is to apply the developmental norms or stages that come with growth. Information processing in childhood proceeds through a variety of stages. It begins with labeling objects in early infancy and moves to devising new ways of handling information such as coding, categorizing, and clustering. If the child persists at the labeling level beyond the normative age, he will be unable to advance to the more abstract levels. As John (28) has pointed out, lower socioeconomic levels do not provide opportunities for learning categorization and clustering techniques. In such cases, the child may become subject to stressors with which he cannot cope, whereas a child from a higher socioeconomic level who has learned these techniques can cope adequately. This inability to cope may be mistaken for an episode of disorder even though the child is otherwise normal.

Four specific markers in the developmental model have been found to be associated with those who develop episodes of schizophrenia. Birthdays in schizophrenics tend to cluster in the winter months (January to March) (22). Some attribute this to a greater fre-
frequency of infectious diseases in neonates during the winter months, others to the possibility that fetuses who pass through the first trimester of pregnancy during the hot summer months tend to have poorer protein nutrition. Findings from studies of the possible role of the mating schedule of the parents have been inconsistent (8).

The influence of environmental and psychosocial events on the central nervous system and their role in producing disturbed behavior have been investigated in several studies. Rosenzweig (50) demonstrated that brains of rats who are limited in their environmental contacts do not develop as fully as those of rats permitted free play and exploration. Deprivation dwarfism, or stagnation of somatic growth and mental development (in spite of normal or even excessive food intake), has been found to be associated with a history of long exposure to emotional neglect. Powell et al. (46) have shown that the release of growth hormone was diminished at the time of admission of such patients, but returned to normal during hospitalization. Thus, emotional neglect can retard physical and mental growth by slowing release of growth hormones. Similarly, Pasamanick (42) has shown that toxemias of pregnancy and other gestation difficulties tend to be associated with a variety of mental disorders in subsequent development.

Kinney and Jacobsen (32) examined the possible association between congenital defects and schizophrenia. They observed a high incidence of ophthalmological defects in schizophrenics and their relatives as compared to other psychiatric patients or normal subjects. Development of friendship patterns during adolescence seems to be an important marker; Dolores Kreisman (34) found that those lacking intimacy tend to be at greater risk for developing schizophrenia.

Mathtotype Markers

If a common factor underlies markers emanating from the learning theory model, it is an inability to develop adaptive behavior or to benefit from past experience. According to Salzinger (53) this results from withholding reinforcement for desirable behavior or reinforcing undesirable behavior. He found that comprehensibility of speech as measured by the Cloze technique was deficient in schizophrenics and that the effect of reinforcement in verbal behavior tended to extinguish more quickly in schizophrenics when the reinforcement was withdrawn.

Singer et al. (57) and Goldstein et al. (18) have examined the possibility that familial interactions may serve as a marker of high risk for schizophrenia. Severe communication disorders between parents and children, especially in tasks like the consensus Rorschach or Thematic Apperception Test, were observed for the families of adolescents who eventually developed schizophrenic spectrum disorders. A speech disturbance scale developed by Gottschalk (19) was found useful in predicting general and psychiatric morbidity.

Chemotype Markers

The internal environmental model claims to have isolated at least four chemotype markers for schizophrenia, specifically, analysis of levels of monoamine oxidase, dopamine-beta-hydroxylase, red blood cell catechol O-methyl transferase, and serum creatinine phosphokinase. Whether these markers are specific to schizophrenia and whether they are linkage markers without any implications for pathophysiology, or whether they are involved in the pathophysiological process of the disorder is still unknown (78).

Neurophysiotype Markers

Many of the neurophysiological markers that characterize mental patients as well as their first degree relatives involve psychomotor control and/or evoked potentials. These include Cancro’s measures of eye movements during visual mental tasks (9), Holzman’s recording of smooth pursuit eye movements (25), the crossover index in reaction time developed by Rodnick et al. (49), and Kornetzky’s and Orzack’s vigilance task of continuous performance (33). Among other proposed neurophysiological markers, the EEG (62) and autonomic markers are prominent.

Shagass (55) summarized much of the evoked potential research in psychiatry and noted that his measure of recovery function in the evoked potential shows changes related to state or severity of illness. He viewed event-related potentials as unproven and perhaps unlikely markers of vulnerability, but added that data from high risk studies have not precluded the possibility that some characteristics of the evoked potential may have high heritability. The most recent results indicate that the P300 component is likely to be an episode marker.

Pupillary reactions of acute schizophrenics and their healthy siblings were studied by Steinhauser and coworkers (64). Most normal subjects and siblings showed a large dilation to auditory stimuli when guessing, and a smaller response when they were certain of the nature of the stimulus. Patients and some siblings failed to show dilation when guessing, and their evoked potentials also were reduced.

In cross-modality reaction time, schizophrenics showed a greater effect under the uncertain conditions than normals, whereas the opposite effect was noted in P300. The significance of this paradox remains to be investigated (39, 67, 70).

One of the recent developments in biological markers occurred in the neuroanatomy of the brain. Because of their relative recency and still tentative nature, they are not treated separately and will be
included with the neurophysiological model. Although anatomical anomalies have been reported since the turn of the century and formed the basis for the establishment of neuropathological laboratories in many mental hospitals, evidence for these anomalies had to wait for technological advances such as the CAT scan. Recently, Weinberger (71) reported that some chronic schizophrenics show characteristic dilatation of the brain ventricles, and Ingvar (26) reported abnormalities in the cerebral blood flow of schizophrenics. Here again, the earlier negative findings have been replaced with positive findings by new technological developments. Similarly, muscle fiber abnormalities and subterminal motor nerve anomalies have been found in schizophrenics by Meltzer (41).

Potential Episode Markers

Markers indicating the onset, duration, and offset of an episode have not been studied as actively as those for vulnerability, but it is imperative that the two be distinguished, since clinical investigations deal with patients during their episodes and only those markers that persist after the episode ends can be considered vulnerability markers. Episode markers, like vulnerability markers, may be classified according to the models or approaches from which they emanate. A review of the contributions for each model reveals gaps that need to be filled.

Descriptive Approach

The descriptive approach, although not a source of actual markers, does provide certain marker-like characteristics claimed to be unique to schizophrenic episodes. Among these are Schneider's first rank symptoms, Jaspers' concept of understandability, and a variety of phenomenologically based claims that eventually could be exploited if established on a more objective basis.

As Hardesty and Burdock (21) have suggested, the profiles of psychopathology obtained with a standardized instrument, such as the Structured Clinical Interview, can be used to determine the presence of an episode, psychopathological fluctuations during an episode, and finally the disappearance of the episode as the profile normalizes.

Genetic Markers

By their very nature, genetic markers should be present before an episode develops and persist after it ends. For this reason, genetic markers cannot serve as episode markers.

Ecology Markers

It has been shown, using the social readjustment scale of Holmes and Rahe (24) that an accelerated rate of occurrence of life events forebodes the development of episodes. This scale also might be used to indicate the end of an episode when the rate normalizes.

The beginning of an episode often follows a period of coping failure. Similarly, once the episode has subsided, one may expect the patient to resume coping at his characteristic premorbid level. Knowledge of the patient's premorbid level of coping ability, if available, could be used to monitor coping effectiveness. Following the behavior analytic model for assessing competence proposed by Goldfried and D'Zurilla (16), Goldsmith and McFall (17) have experimented with simulated interpersonal contexts to evaluate the effectiveness of patients' social coping strategies. The entire spectrum of role performance actually should be sampled to see whether the capacity to cope has returned to its premorbid level. Weissman (73) recently reviewed 15 scales available for assessing performance in occupational, marital, extended family, and community roles. These might aid in probing for fluctuations in coping capacity that occur during hospitalization, particularly if it were possible to simulate the significant role contexts.

Developmental and Learning Markers

The speech and thought processes of the patient, which may be highly dependent on learning and reinforcement, often are found to deviate from the usual during an episode. Monitoring the speech and thinking characteristics at the onset, during, and at the end of an episode can provide useful markers. Schmale (54) suggests that giving in to feelings of helplessness and hopelessness is the earmark of a beginning episode. Luborsky and Auerbach (40) have derived another potential mini-episode index by examining speech samples of patients in psychoanalysis taken just before instances of momentary forgetfulness or just prior to reports of migraine headaches or stomach pain. When these passages are rated for content, helplessness ratings are much higher than for samples taken at other times during therapy sessions. It is possible that mild transient mini-episodes also might be provoked experimentally by psychological or biochemical challenges. Such probes might provide a basis for determining whether the major episode is still present. The ethics of such experimental procedures must be carefully investigated, of course.

Internal Environment Markers

Janowsky et al. (27) have shown that if ritalin is injected in a patient undergoing an episode of schizophrenia, the episode will worsen briefly, but that if the episode is no longer present, no exacerbation is induced. Another strategy for determining the state of the episode may be to monitor mini-episodes or acute
periods of symptom exacerbation in patients during their hospital stay. These may, in microcosm, reveal properties of onset and offset in mini-episodes. Although most of the progress in this area has concerned a search for indicators in depressed patients, it is likely that comparable indices can be found for schizophrenic mini-episodes induced by visitors, peer conflicts, and so on. In a study of the rise and fall of corticosteroid levels in reactive depression, Sachar and co-workers (52) observed that hormonal stress levels rise when the patient actively struggles with the confrontation of the loss of a love object or when his defense mechanisms falter temporarily. On the other hand, when his defenses are adequate and he seems clinically comfortable and adjusted, the hormonal level drops to normal. After the patient has adjusted to the hospital regime and achieved stable hormonal levels, perturbations in corticosteroid levels may therefore index the eruption of mini-episodes.

Neurophysiological Markers

Findings in depressives indicate that changes in sleep characteristics (35) and motility (36) mark the beginning and end of episodes. In schizophrenia, too, a reduction in rapid eye movement sleep accompanies acute episodes (37). The amplitude of the P300 component in evoked potentials also is likely to prove an episode marker (55). Comparing skin conductance and heart rate during reaction time studies and arithmetic tasks in acute schizophrenics, Zahn et al. (76) found differences for patients who improved over a 4-month period, whereas those who failed to improve showed an autonomic profile similar to that of chronic schizophrenics, suggesting that these measures may be episode markers.

Research in Vulnerability

Research efforts inspired by the vulnerability model have been underway for several years. A series of ongoing studies in vulnerability, initiated by the senior author while chief of the Biometrics Research Unit at the New York State Department of Mental Hygiene and continuing under the direction of Samuel Sutton (66), have suggested several potential markers. This research is summarized briefly below.

The vision laboratory, headed by Mitchell Kietzman (31), has collected detection threshold data in two studies of 55 schizophrenic and depressed patients, 15 siblings of schizophrenics, and 31 controls. Approximately half of the patients showed higher thresholds (were less sensitive) than the siblings and controls. Semistructured interviews indicate that the rating on the scale for auditory hallucinations correlates significantly and positively with higher visual thresholds. Since results were obtained with a forced-choice tech-

nique, the response criterion or bias problem was eliminated. Although this technique does not compensate for the possibility of reduced attention or motivation, variability within each subject was the same for patients and controls, suggesting that the two groups were equally attentive and motivated.

In the audition laboratory, headed by Gerald Brueder, differences were found between schizophrenics and normals on the one hand, and affective patients on the other. The thresholds for paired clicks, one presented to the right ear and the other to the left ear, were compared to thresholds for single clicks to each ear alone. The interval between the paired clicks was 60 msec. Normals and schizophrenic patients showed a slightly greater gain in sensitivity when left ear clicks preceded right ear clicks in the paired presentations (compared to each ear presented singly) than for the reverse sequence. In contrast, affective patients showed the opposite pattern—greater gain in sensitivity when right ear clicks preceded left ear clicks. The data are consistent with the assumption of a left hemisphere dysfunction in affective patients. No evidence was found for the previously reported left hemisphere dysfunction in schizophrenic patients. Although this finding is primarily useful as a potential marker for affective disorder, it can serve as a negative indicator for ruling out schizophrenia.

Data from the evoked potential laboratory, headed by Samuel Sutton, suggest that the P300 component of the event-related potential has a smaller amplitude in schizophrenics and in depressives than in normals. This is probably an episode rather than a vulnerability marker. The amplitude of P300 tends to return to normal during periods of remission. Whether it becomes entirely normalized is not yet clear. There is some evidence that the pattern of augmentation or reduction as a function of stimulus intensity, reported by Buschbaum, may indeed be a vulnerability marker.

Augmentation is the tendency for the amplitudes of early components to increase as the intensity of the stimulus decreases and reduction is the opposite tendency, for the components to decrease with the increase in intensity.

In the pupillography laboratory, headed by Gad Hakkerem, reduction in the amplitude of pupillary contraction to light and related dilations to the onset of darkness has been confirmed for schizophrenics as contrasted with normals. Data indicating that such response decrements are maintained even after the end of an episode suggest that pupillary response may be a vulnerability marker. Most studies discount the influence of phenothiazines on pupillary contraction, although scattered reports suggest that long-term phenothiazine administration may produce additional temporary reduction. Schizophrenics also show marked deviation in psychosensory dilation to non-


ual stimuli (pupil contracts only to light and pain; to other stimuli it dilates).

Summary

Schizophrenia today is no longer the deteriorative disorder it appeared to be in the first part of this century. Most schizophrenics today spend the greater portion of their lives in the community, and when the community begins to provide better facilities, perhaps only 6 to 10 per cent will remain chronically ill.

The vulnerability model assumes that schizophrenia is not a continuous disorder, but that vulnerability to it is. This vulnerability may remain latent for life, or be elicited by life event stressors. The sources of vulnerability are to be sought in the various etiological models. Markers for identifying vulnerable individuals could be provided using the techniques developed in the investigations initiated by each of these models. Although the impact of a life event stressor induces crises in everyone, only those in whom the stress falls below the vulnerability threshold can absorb the crisis homeostatically. When the stress exceeds the threshold, the crisis develops into an episode. As soon as the stress and its aftermath wear off, the episode ends and the person returns to his premorbid adjustment level. Therapeutic intervention should be directed not at curing the disorder, since it is self-limiting, but at ameliorating the suffering and at preventing its initial occurrence or its recurrence.

To attain this goal, markers are needed by which the vulnerable can be identified. Each of the etiological models therefore should be investigated to provide indicators by which the etiological factors can be determined. Once such markers become available, it may be possible to detect individuals prone to schizophrenia even before episodes occur. Careful monitoring of such individuals should provide information on life contingencies that trigger episodes. Prophylactic intervention through education, self-monitoring, or therapeutic intervention can then abort incipient episodes and prevent their recurrence, as is the case with conditions such as allergy or diabetes.

Thus, to break the current logjam in schizophrenia, a three-pronged attack should be launched: a) discover vulnerability markers; b) follow a group of vulnerable individuals to determine what contingencies trigger episodes; and c) apply this knowledge in preventing initial and recurrent episodes in the vulnerable.

References


