Kraepelin (1), following Karl Kahlbaum’s lead, regarded dementia praecox as a disease entity (to be distinguished from the patient’s psychopathological state) and regarded the patient as portraying a collection of core symptoms. He minimized idiosyncratic and particular features and concentrated on what he believed to be the core symptoms (2).

He bemoaned the fact that the knowledge then current of neuroanatomy, physiology, biochemistry, psychology and pathology was inadequate to serve as a basis for etiology and nosology, a deficiency which still holds true today.* Kraepelin’s original classification is essentially still in use today and in fact, after an interregnum in which psychodynamic theory held sway and sideswiped Kraepelin’s contributions, the pendulum has swung back to a neo-kraepelinian era in American psychopathology.

The return to Kraepelin was brought about by the new developments in biological approaches to etiology which required a firmer basis for classification. As a result, schools and laboratories developed zealous researchers in at least 7 etiological models of psychopathology: environmental (including the ecological, developmental and learning models) and the biological (including genetic, internal environment, neuropsychological and anatomical models) (4, 5).

From the very beginning, the search for the causes of dementia praecox took on a biological trend. Kraepelin himself, imbued with the discovery of the biological source of general paresis, hoped to find a corresponding toxin for schizophrenia. He did not ignore psychological and psychosocial-cultural factors but did not regard them as primary causes. Thus, although he hoped to discover the borderline between mental health and disease by means of psychological tests** he probably regarded performance on these tests as reflecting the results rather than the basic cause of the

* It is interesting to note that Joseph Goldberger held the same opinion. After achieving his well deserved fame by unravelling the dietary origin of pellagra with psychosis, he was offered a grant to unravel the mystery of schizophrenia. He declined the offer for the above reasons (3).
** ‘As soon as our methodology has sufficiently proved itself through experience with healthy individuals, it would be possible to approach the actual ultimate goal of these efforts, the investigation of the sick personality, especially of the inborn pathological disposition . . . We, therefore, have first of all to investigate whether it is possible by means of psychological tests to determine individual deviations, which cannot be recognized by ordinary observation. If that succeeds, we would be in the position through the quantitative determinations at our disposal to establish the borderline between health and disease much more precisely and more validly than has been possible so far.’ (6)
disorders. Similarly, although he was interested in cross-cultural studies (7) he again regarded social-cultural forces as secondary. Accompanying Kraepelin's search for toxins was the search for anatomical anomalies in the post-mortem dissection of brains of schizophrenics conducted by Alzheimer in his clinic utilizing the special staining dyes of Nissl. Both of these attempts were to no avail and the biological search came to a standstill temporarily.

As Derek de Solla Price (8) has pointed out, great discoveries in medicine as well as in science in general often come not from theorists but from inventors who open up new vistas by such devices as telescopes and microscopes. But not all progress comes from general technological advances. Some progress comes from direct attacks on the problem with serendipity often playing an important role. The search for the biological causes of schizophrenia benefited from both new technology as well as from direct attack and serendipity. Thus, the methods for brain imaging provided by new scanning methods (CAT scans, MRI, etc.) have led to the detection of enlarged ventricles and brain atrophy in some schizophrenics, while the serendipitous discovery of the effect of neuroleptics and the role that dopamine receptors play in their efficacy led to a veritable revolution in biological approaches. But here too, certain prior discoveries paved the way. Among these were Loewi's (9) classic experiment demonstrating that synaptic transmission between neurons was primarily biochemical rather than electrical in nature and the serendipitous discovery of the effect of LSD-25 on both brain metabolism and simultaneously on overt behavior that led to the investigation of the effect of drugs on brain function and behavior (10). The discovery of such drugs as dilantin (phenytoin), affecting epileptic seizures, lent more hope to finding similar drug effects in schizophrenia. Even drugs like insulin and metrazole (pentetrazole) which finally fell into disuse added to the enthusiasm for the biological search for etiology. In addition to the anatomical and biochemical findings regarding the probable causes of schizophrenia there were the older findings of genetic inheritance and of neurophysiological deviations in schizophrenic responses to controlled stimulation (11). However, even the most etiological model provided by genetics did not turn out to be both a necessary and sufficient cause, as evidenced by the rather low concordance in monozygotic twins as well as by the presence of phenocopies.

With regard to the neurophysiological model, most of the effort has been directed not so much at etiology, but more indirectly at finding markers which would identify the individuals who are at risk for developing schizophrenia.

On the opposite end of the biological spectrum are the ecological model, the developmental model and the learning theory model which some researchers have considered as including causal agents in schizophrenia. During the recent rise of interest in the biological end of the spectrum there has not been as striking an advance in the research on the environmental end of the spectrum except for two outstanding findings: (a) the role of social networks as buffers or exacerbators in the development of schizophrenic episodes (12) and (b) the role of the family environment focusing on high and low emotional expression (13). These two factors, while not as dramatic as the factors of brain imaging and biochemical brain disturbances in relation to the production of episodes, have nevertheless made a deep impression on the field.
The learning theory model gave rise to the school of behavior modification which has demonstrated its usefulness in modifying psychopathological behavior but there is no great claim being made for this model as being causal in the development of schizophrenia, though attempts at instituting circumscribed psychopathological behaviors or symptoms by means of learning theory methods have proven successful (14). In general, the learning theory approach does not postulate a causal agent for schizophrenia since it regards it not as a disease but as a collection of deviant behaviors developed under the influence of reinforcements of various types (15).

In summary, we have indicated that biological factors and environmental factors are somehow involved in the development of schizophrenia but no single factor in itself is necessary and/or sufficient to produce an episode of illness. There seems to be a need for some integrating model which could contain the extant models as submodels and permit them to interact in the production of an episode. The vulnerability model is potentially capable of enclosing all the etiological models within its fold and explain many of the contradictions we find in the field of schizophrenia.

The Zeitgeist seems to determine the acceptable models of the day. Prior to Kraepelin's day, one of the most influential models for the etiology of mental disorders (including the still to be named dementia praecox — schizophrenia) was the degeneration model (16). With the advent of Kraepelin, who had been influenced by Wundt's psychophysiology, an interest in the physiological underpinnings of schizophrenia became popular. As the sciences progressed, genetics, internal environment, neurophysiology and neuroanatomy provided more sophisticated etiological models. But the belief in the dire outcome of mental illness associated with the degeneration theory persisted in the folklore despite scientific disavowals. This pessimism persisted even in the face of the benign long-term follow-up studies of Bleuler (17), Ciompi (18), Huber (19) indicating that deterioration was not in store for most schizophrenics but rather an opposite outcome was more likely. The only explanation for the persistent pessimism is the biased sample which confronted most practitioners. Even E. Bleuler's pessimism regarding outcome was attributed by his son, Manfred, to the bias produced by dealing primarily with the recidivist chronic patients, while those who no longer needed the clinic were less likely to receive the attention of researchers (17).

The need for the concept of vulnerability as opposed to disease is inherent in the genetic model, since penetrance of a gene is rarely 100%. There is, therefore, a need for a term to designate the unexpressed genotype (the unaffected carrier of the gene(s) for schizophrenia), as opposed to the expressed genotype or phenotype. Designating the unexpressed genotype as a vulnerable individual* seems to satisfy the above need. Perhaps the most striking historical example for the need for the concept of vulnerability is provided by the dramatic performance of Max van Pettenkofer who conducted a public experiment in which he and some of his students consumed cholera bacilli. Neither he nor his students contracted the disease (21). Presumably, they were either invulnerable to cholera or the contingencies needed for cholera to develop were missing.

* Zubin et al. (20) have suggested the term 'schizotrope' to designate a person vulnerable to schizophrenia.
The fact that concordance in monozygotic twins was far from 100% gave rise to the diathesis stress model promulgated by Paul Meehl (22), Rosenthal (23), and Zubin (24). In these models, the presence of the inherited propensity was by itself not enough to convert the genotype into a phenotype and the need for a triggering device in the form of some type of stressor to elicit the vulnerability had to be introduced.

A striking example of the need for a stressor to elicit vulnerability is offered by Pasteur’s experiment in which chicks were inoculated with anthrax bacilli but failed to develop the disorder until they were subjected to the stress of being thrown into freezing water. Then the bacilli were triggered into action (25).

In contrast with the disease model of schizophrenia as laid down by Kraepelin, the vulnerability model is non-kraepelinian. It does not presuppose the existence of an underlying disease process (something which it has in common with the learning theory model). It does, however, differentiate the schizophrenic from the normal by postulating a permanent predisposition to the development of an episode which will appear under certain contingencies as explained before.

DEFINITION OF VULNERABILITY

There are quite a number of cognate concepts similar to the concept of vulnerability which should be differentiated from the vulnerability concept itself by noting the similarities and differences that exist between them. Among the cognate terms are risk, susceptibility, liability, proneness, exposure, endangered, and predisposition (26).

Risk has been defined either in terms of patient characteristics or environmental factors which place certain individuals at a higher probability risk of developing a disorder than the general population (27).

It might be well to limit ‘risk’ to environmental factors and use vulnerability as a characteristic of the individual. Susceptibility seems to imply both personal vulnerability as well as environmental risk; liability, proneness, exposure, and endangered belong in the same category. Predisposition seems to belong with individual vulnerability.

Not all schizophrenics have family histories positive for schizophrenia and this has led to their designation as sporadic schizophrenics or phenocopies, having acquired rather than inherited schizophrenia. A question arises regarding the meaning of the term ‘acquired vulnerability.’ It is difficult enough to conceive of how even genetically based vulnerability develops, but here at least we can postulate the existence of an inborn deviant allele or alleles in the genome which sets into motion the processes leading to the development of an episode. But what can we say about non-inborn or acquired vulnerability? Suppose we postulate a viral cause.* How does the virus bring about its effect? Presumably under this condition, schizophrenia must follow a path of development different from the genetic path and yet lead to an end result which is a phenocopy. Can a phenocopy also be produced by

* An interesting hypothetical answer to this question is provided by T. Crow (28) in the form of a retrovirus.
the presence of long enduring stress in a noxious niche such as is provided by underprivileged ghetto existence? Toxic environments of this type are often alienating, lonely and sometimes downright frightening (29). Can they too, utilizing another pathway, produce a schizophrenic phenocopy not dependent on the DNA equipment the person is born with? Perhaps acquired vulnerability is only a metaphor in actuality occurring only in individuals with an inborn (genetic) propensity in whom the usually protective moderating variables (prenatal personality, social network, ecological niche, etc.) are incapable of providing the required protection while their first-degree relatives are free of schizophrenia because of this protection. Is this why these psychosocial factors seem to be blamed for producing the episode when in fact they only produce the stress needed to trigger the episode? This stress need not be acute. Maybe, in the case of acquired vulnerability there is no need for a trigger, the episode setting in, gradually, by continual accretion of the stress until the ‘cup runneth over.’ To consider such individuals as phenocopies simply because they have no apparent family history, is not entirely satisfactory unless the matter of penetrance is considered. The proportion of schizotropes (carriers of the genotype for schizophrenia who have not yet or never will develop the phenotype) has never been accurately determined, but estimates of the ratio of unexpressed to expressed genotypes run as high as 3:1 (23) and in order to establish sporadicity, at least 21 first-degree relatives must be found who are free of schizophrenia (Zubin, unpublished data).

Whether the genetic variety of schizophrenia and the various phenocopies are basically the same or whether they represent different subtypes of schizophrenia with varying characteristics and outcomes is still an open question. For the sake of parsimony it might be well to assume that they are all of the same cloth until we are forced by the data to assume otherwise.

In addition to vulnerability markers and episode markers, there are several more indicators that need to be taken into consideration. Some indicators do not exist in the pre-episode period but develop during the course of the episode and do not disappear when the episode ends. Among these are the so-called negative symptoms which are often referred to as residual symptoms (or deficits). It is still to be determined whether they are indigenous to the disorder or result from iatrogenic, nosocomial, or ecogenic factors. This is the heart of the chronicity problem.

There are also certain characteristics that usually appear when an episode is imminent. These harbingers are not invariably followed by an episode and therefore can not be regarded as markers, but as predictors of a possible approaching episode or as prodromal. There are also some indicators that are prognostic of outcome. Thus, Tsuang (30) has pointed out that in a study of 200 schizophrenics meeting Feighner research diagnostic criteria, followed up 30–40 years after their admission, the following characteristics present at the time of admission predicted chronicity or poor outcome: memory deficit, thought blocking, social withdrawal, auditory or visual hallucinations and younger age of onset.

The following characteristics led to good outcome, euphoria, hyperactivity, flight of ideas and persecutory delusions. An overall review of prognostic factors in schizophrenia is provided by Zubin et al. (31) covering some 900 studies in the literature. The most striking finding was that good premorbid personality led to good outcome.
Some indicators may be present in excess of chance expectancy only in unaffected first-degree relatives of schizophrenics but not in the probands themselves. They present an interesting possibility. Perhaps they are indicators of invulnerability, a characteristic that is antithetical to schizophrenia even as Meduna thought epilepsy was. Thus, though the first-degree relatives may share other vulnerability markers with their probands, the presence of the invulnerability marker counteracts the vulnerability indicated by the other markers and cancels the vulnerability of the individual. Similarly, the marker that is absent in first-degree relatives in a proportion significantly below that in the general population, but is present in the probands in pre-episode, episode and post-episode intervals, may identify the individuals who are resistant to being vulnerable to schizophrenia. Had this marker been absent in the probands, they too might not have been vulnerable, even though they may have had other vulnerability markers. A search for such markers would indeed be a worthwhile endeavor.

In contrast with vulnerability, episode, residual and prodromal factors there are some variables that can either increase or decrease the probability of a disorder developing in vulnerable individuals. Among these are premorbidly present personality traits unrelated to the disorder but capable of either raising or lowering the probability of a disorder developing. The social network may act in a similar manner to either mitigate or enhance the probability of a disorder. The ecological niche that the person occupies in life may also be either protective, or provoke the development of disorder. These are the moderating variables referred to earlier.

The vulnerability model as promulgated by Zubin (24) belongs to the general class of diathesis stress models but differs from the other models of this class by specifying the role of such parameters as (a) specific triggers in eliciting an episode in the vulnerable; (b) the role of moderating variables such as premorbid personality, ecological niche and social network in determining the onset and outcome of illness; and (c) the episodic nature of schizophrenia in contrast to the generally accepted chronic presence of the illness after onset. Furthermore, the vulnerability model has launched a search for markers of vulnerability and of episodes and has formulated the need for other types of markers which the model requires. In addition, investigation of such triggers as life events and of the moderating variables modifying their impact on the vulnerable have also been launched.

How did the vulnerability hypothesis come into being? Aside from the biblical reference which had a Lamarckian tinge ‘The fathers have eaten a sour grape, and the children’s teeth are set on edge’ (Jeremiah, 31:29—30), the first mention of the vulnerability theory which I have been able to find is due to Karl Friedrich C. Canstatt (1807—1850).* In dealing with the ‘causes of psychoses’ he states:

“One can observe in many subjects, who may not be directly labelled mentally ill, such a high degree of psychic agitation/activation (‘Erregung’), that only a small event (‘Anlass’) may be sufficient to produce manifest true alienation. We call this psychic vulnerability. And most of the occasional causes provoking manifest mental illness already find this predisposition’ (32).

* Professor Dr. C. Scharfetter has kindly called my attention to this early mention of vulnerability and has provided the translation from the German source.
The second mention of the vulnerability concept using the term predisposition goes back to Griesinger (33) who wrote: *'If one considers the extraordinary frequency of all the noxious influences which are put forward as causes for mental illnesses and, at the same time, considers the relatively infrequent emergence, which follows those influences, one necessarily reaches the assumption that certain predisposing circumstances are indispensable, in order to bring about an illness and just this specific one at least in some instances; in other words, that a certain susceptibility and disposition for that kind of disturbance clears the way for the triggering causes, which are sometimes not very marked in severity.' Some of Kraepelin's early writings, as I indicated before, also referred to vulnerability and even Freud had some reference to it when he pointed out that repression is not causally sufficient for neurosis but that hereditary vulnerability is causally relevant (34).

The fact that two writers in the 1840s referred to the same concept of vulnerability would lead one to believe that the concept was in the Zeitgeist and generally well known. Why it dropped out for nearly a century is an interesting question for the history of science. It is as difficult to trace the roots of a developing concept as it is to trace the origins of a river, since many tributaries, springs and run-offs contribute to its final course. In retrospect, the driving force which led to the development of the concept of vulnerability was the realization that phenomenology alone in the form of descriptive psychopathology was only the surface appearance of the mental disorder and gave no clues as to its origin. In searching for the etiology of schizophrenia, which was the major focus of the vulnerability theory, all the various schools of etiology from the purely environmental to the purely biological were examined. The available techniques for testing the tenability of models through psychobiological tests were found to be neither sufficiently reliable nor valid. This led to the development of a Mendeleeev-like table of the relationship between stimuli and responses in schizophrenics as contrasted with normal subjects (11). The stimuli were classified on one axis as energy, signal or symbol stimuli and the responses on the other axis as physiological, sensory, perceptual, psychomotor, and conceptual (now called cognitive). This table provided a systematic experimental approach to determine the patterns of stimulus—response paradigms which differentiated schizophrenics from normal subjects. This strategy seemed to open an entirely new approach, which was designated as the biometric approach. The models included in this approach (4) have already been described. Was there a common factor running through these models? I realized that each model had a place in the etiology of schizophrenia but that a superordinate model was required to make room for all seven models. The vulnerability model was the result.

Its final formulation was greatly influenced by our contacts with European psychiatrists which began with the US/UK Project on Diagnosis (35). Sir Aubrey Lewis’ stress on the psychosocial factors, especially as represented in Wing’s (36)

* The author is grateful to Professor R. Olbrich for bringing the Griesinger quote to his attention and for editing the translation. Professor Dr. C. Sharpeter comments that Griesinger never used the term 'vulnerability' but instead used the term 'predisposition' which he compared with 'irritable weakness.' The term 'predisposition', he points out, was used long before Griesinger used it. Thus, the priority for the use of the vulnerability concept needs to be investigated more thoroughly by historical approaches.
work, Essen-Möller's (37) personality, diagnostic and genetic studies, Strömgren's (38) epidemiological work and Bleuler's (17) long-term follow-up studies (to which I was exposed only after 1972) all had their impact. In the United States, Morton Kramer's (39) epidemiological studies, Franz Kallmann's (40) genetic studies, Paul Hoch's (41) diagnostic studies and Carney Landis' (42) experimental psychopathological studies helped shape the eventual development of the theory.

The most recent impact of the long-term follow-up studies of Bleuler, Ciompi and Müller, and Huber helped give the more optimistic tinge to the theory. My original proposal for the vulnerability theory was given in an address at a Symposium on Behavioral Concomitants of the Mental Disorders before the Department of Psychology at McGill University in 1960 and appeared in an obscure journal (24) about the same time as Meehl's (22) seminal article and subsequently Rosenthal's article (23) on the diathesis stress model. Unfortunately, we had not been aware of their work at the time, but our subsequent work on the topic benefited from the more general theory of the diathesis-stress model, especially Falconer's (43) formulation. The special characteristics which differentiate the vulnerability from the general diathesis-stress model have been indicated in the following quotation from Zubin and Spring (44):

'Why then is this article necessary, if its main thrust has been anticipated by several earlier publications? (22, 23, 45, 46) The answer lies in the fact that although the data on which vulnerability was based are known, their organization and application have lagged. Further, although vulnerability has been proposed several times, it has never caught on in schizophrenia. We have arrived at this formulation independently of our predecessors, driven to it not by the weight of evidence that has accumulated but by the way in which it illuminates the meager evidence. In addition, we have suggested biometric approaches for testing the tenability of the vulnerability model by indicating the need for measures of life event stressors, competence, coping, and vulnerability to schizophrenia as well as markers of the onset and offset of schizophrenic episodes.'

The search for markers has recently received a new impetus by introducing the consideration of information processing into the search.

TESTING THE TENABILITY OF THE VULNERABILITY HYPOTHESIS

To test the tenability of the vulnerability model is not an easy undertaking since it involves determining: (a) who is vulnerable and the degree of vulnerability; (b) the triggering factors that elicit the vulnerability; (c) the factors that protect individuals who though vulnerable never develop episodes (e.g. unaffected co-twins of probands who develop an episode); (d) the factors that bring about a termination of the episode after it develops and (e) the factors that lead to either relapse or exacerbation. To carry out a program for answering all of these five questions is a formidable task. Consequently, we have directed our attention initially to two major questions: who is vulnerable and how do recidivists differ from those who have only one or a few episodes and recover.
The parameters and the underlying processes of the vulnerability hypothesis

In order to test the tenability of the vulnerability hypothesis it is necessary to specify its underpinnings and indicate the various parameters and processes involved in the construction of the hypothesis. At this stage of our knowledge, all we can do is hypothesize these elements since we have little recourse to observations or data yet.

By vulnerability itself we mean a trait characterizing the individual which under a certain provoking or eliciting contingency will manifest itself by the development of an episode of illness. Thus, the vulnerability trait is presumed to remain constant throughout life but the provoking or eliciting agents as well as the moderating agents may change in time, becoming stronger or weaker in their potentiality to elicit the episode or to abort it.

The indicators required to identify the schizotrope must be relatively independent of the pathophysiological processes involved in the episode. If that were not the case, the indicator might conceivably indicate the beginning of an incipient episode, i.e. a prodromal indicator. The ideal indicators would be linkage markers, or in the end of our search perhaps the morbid alleles themselves, which would remain latent unless provoked by a triggering stressor.

The triggers might be any stressor that increases the probability of eliciting an episode. It may be an external event such as a dramatic life event, an internal event, perhaps some change in the immune system involving stress or it may be some type of continuing irritation or disturbance which finally reaches a threshold of stress sufficient to elicit an episode.

What is meant by a stressor? To elucidate this parameter we need to turn to the definition of stress which has proved so useful for our purposes. Our definition follows the discussions of Zubin and Spring (44), Wilkins (47), and Gross (48). They regard stress as occurring as a result of ‘the failure of routine methods for managing threats.’ Mechanic (49) indicates that stress arises when ‘(...) a discrepancy (develops) between the demands impinging upon a person — whether these demands be external or internal — whether challenges or goals — and the individual’s potential responses to these demands.’ Lader (50), in a similar vein indicates that stress occurs when stimulation raises the activity of the organism more rapidly than adaptation can lower it. But what does adaptation consist of?

Adaptation*

Adaptation or the ability of an individual to respond adequately and appropriately to life’s exigencies is a concept with a long history and extensive literature and it would be out of place to try to summarize it here. However, it is necessary to analyze adaptation into its components if we are to use the concept in our discussion of vulnerability.

In looking for an analysis of adaptation we found Lois B. Murphy’s analysis most useful (51). She points out that adaptation ‘(...) involves (a) reflexes (built-in mechanisms) and instincts (broader built-in patterns); (b) coping efforts (to deal

* This discussion of adaptation and coping is adapted from Zubin and Spring (44).
with situations not adequately managed by reflexes; (c) mastery resulting from effective and well-practiced coping efforts; and (d) competence as the congeries of skills resulting from cumulative mastery achievement.’

She goes on to point out that reflexes and instincts do not go far in dealing with life exigencies viz. demands, threats, and opportunities that life offers. Consequently, man is required to engage in coping, that is, constant invention and incessant trial-and-error stabs at adapting, to supplement the limited (if impressive) repertoire of reflex capacities. This coping process may lead to direct solutions of the presented problems or to circumventions via defense mechanisms such as denial, projection, etc. A further distinction can be made between the capacity to deal with the normal opportunities, frustrations, obstacles of the environment or routine coping, and the capacity to retain internal equilibrium or homeostasis despite internal and external disturbances of a catastrophic character. It is the breakdown of the second type of coping that leads to an episode.

The reflexes or built-in mechanisms utilized in adapting to life circumstances are exemplified by such responses as the dilation of the pupil in darkness and the tonic neck reflex of the baby. The instinctive or broad built-in or developed patterns are exemplified by nest-building in animals and maternal behavior in humans. Coping efforts are exemplified by the persistent application of energy towards the solution of tasks involving problem-solving and abstract thinking in situational dilemmas. Mastery refers to the mechanism of overcoming difficulties through coping and represents the integrating factor in adaptation. Competence represents the skills and capacities developed through exerting coping efforts in the solution of problems and consists of social skills, intellectual strategies and other acquired capacities equipping the individual to deal with life exigencies.

In the growth of the individual, the adaptive capacity for meeting life exigencies develops gradually as his coping efforts emerge from their genetic and maturational matrix. These coping efforts crystallize into routine procedures as they are rewarded with success in life. They constitute an important part of primary personality in the non-schizotrope and also an important part of the premorbid personality of the schizotrope who attains phenotypic expression. However, when a calamitous stress-producing stressor appears, routine coping efforts may not be adequate and new tactics and strategies may be needed. In simpler environments the meeting of such traumatic stress-producing events was routinized by cultural sanctions and practices which rarely led to deviant coping or, if it did, such deviations could be contained by proper institutional forms. Thus, traumatic life events were dealt with in a routinized conventional manner so that even the deviant grief behavior could be contained within normative bounds. In our own culture, responses to catastrophic life events are not always easily channelled into institutionalized forms. While most of us tend to find suitable coping strategies in emergencies, some, the most vulnerable, do not always find suitable coping strategies and this is where an episode might develop.

The coping effort is not to be confused with competence. By coping is meant the attitudinal motivational stance which a person assumes when faced with a task. He may exert his best efforts and intense zeal in arriving at a solution. Competence, on the other hand, refers to the accumulated know-how, cognitive abilities and skills
needed for solving a problem. In a sense, coping represents the motive power of the organism while competence represents its capacities or, in computer terms, coping is the software and competence the hardware.

We might liken coping ability to the voltage of the electric current that sets a motor into operation. The motor may be unchanged but, unless the voltage is maintained within proper limits, the operation of the machine will be interfered with. Thus, a drop in line voltage will produce an 'episode' in the machine and a drop in coping ability will similarly produce an episode in the person.

We might now raise the question as to which of the four components of adaptation falters when an episode of schizophrenia develops. It is unlikely that reflexes and instincts are lost by the development of the disorder nor that competence is destroyed by it, since both of these components reappear in their original effectiveness after the episode ends. Mastery is not really a component of adaptation since it is the mechanism through which competence is built up and is reminiscent of White's sense of efficacy and Maslow's mastery concept. This leaves the coping effort as the likely candidate for disruption when an episode develops.

Unfortunately, we have no direct access to measuring coping ability and must judge it via performance which involves the other two components.

Granted that coping ability is the culprit in a schizophrenic episode, the question arises just how does it go wrong. Corresponding to Murphy's two coping levels, Lazarus et al. (52) distinguish between 'healthy positively adaptive problem-solving efforts characteristic of low-stake situations and the primitive and maladaptive forms of coping typically associated with conditions of high-stake (that is, severe threat, frustration, conflict and great challenge). It is this switch from normal coping with the exigencies of everyday life to coping with catastrophic situations that may mark the beginning of an episode. We do not know whether catastrophic coping is a continuation, albeit in exacerbated form, of routine coping, or whether it represents a totally different type of coping effort reminiscent of Kurt Goldstein's catastrophic reactions. How to find markers for this shift, indicating the onset of an episode, is our problem, and how to determine when coping ability returns to its normal level after the episode ends is another problem we must face.

In surveying the literature on adaptation we find very little discussion of the problem of shift in coping level. We did find, however, considerable discussion of the types of coping that are observed in everyday adaptation. But we are not concerned with the typological analysis of everyday coping. We are concerned, however, with what happens when an individual undergoes a catastrophe which often precedes an episode of illness -- the helplessness and hopelessness it brings on, and what objective markers, if any, can we find distinguishing the change in coping?

One example of the shift is offered by Falek and Britton (53). They postulate that there are four states in coping under stressful situations: (a) shock and denial; (b) anxiety; (c) anger and/or guilt and (d) depression. These increasing states of disturbance push out of balance the physiological and psychological homeostasis and in the psychological sphere lead to the breakdown of such factors as self-esteem, social relations and occupational adjustment. Unless the person can reinstate his psychological homeostasis an episode will develop. Similar analyses of the physiological homeostasis leading to an episode can also be noted.
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What do we mean by an episode? In non-schizotropes, stressors also bring about some change in behavior and feeling but the homeostatic mechanisms in such cases absorb the stress and the individual returns to his pre-crisis balance. In the case of schizotropes the triggering stressor may produce a disturbance of homeostasis which does not return to its pre-crisis level of balance but erupts into a disturbance which produces deviant behavior and emotional disturbances beyond the control of the individuals or their homeostatic mechanisms. Schizotropes usually first respond with a variety of coping strategies to deal with the crisis which may be either successful and gradually contain the stress, or be unsuccessful and eventuate into an episode. If they are successful, we regard it as a spontaneous recovery which may never be reported and may go unnoticed. If their coping strategies fail to contain the disturbance, an episode of illness ensues which usually brings the individuals to the attention of their peers who may provide treatment or let them continue in their state of disarray.

What are some of these coping strategies which are elicited by a triggering stressor in a vulnerable individual?

Coping strategies develop in infancy and early childhood under the impact of maturational states and environmental forces, especially those dependent on the family. In that sense, they are part of the primary personality development in the non-schizotrope and part of the premorbid personality of the schizotrope who develops an episode. It is clear that the primary and the premorbid personality have genetic as well as environmental sources, but they develop independently of the vulnerability aspects of the individual. While the incidence of schizophrenia is found to be associated with premorbid personality (54) the association is rather mild. Some of the coping strategies which have been studied are denial, withdrawal, and avoidance, but there are also strategies of throwing oneself into a task with great vigor, searching for avenues of expression to rid oneself of the disturbance brought on by the episode, basic efforts to compensate for disabilities imposed by the episode and similar contrivances. In these ways the schizotropes tend to defend themselves against the impact of the disturbance. Thus, both the various defense mechanisms as well as achievement drive, self actualization drive do battle with the psychosis.

It should be noted, however, that not all the schizotropes invariably develop episodes when a sufficiently potent stressor impinges. Those schizotropes who have good social networks, good premorbid personalities, and occupy satisfactory niches in life may find these moderating factors as protective cushions aborting the stress. Instead of a full-blown episode, they may escape with a temporary crisis which the homeostatic mechanism copes with successfully. The coping phase has been described under the concept of natural self-healing which dates back to Hippocrates (55) and has more recently been described by Böker (56):

‘On the foundation of such a descriptive model, self-healing attempts can be understood as efforts on the part of vulnerable persons at self-stabilization when their psychic equilibrium threatens to collapse as a result of stresses of internal or external origin and when routine coping behavior is unsuccessful. Such a theoretical perspective fits the clinical impression that numerous schizophrenic patients regularly demonstrate more or less clearly a temporary disorganization
of behavior when they feel themselves to be in threatening situations of stress. They experience — so to speak — psychotic ‘mini-episodes.’ Why and how they succeed in most such cases to avert a serious psychotic breakdown and how they resume normal coping behavior after having once more regained equilibrium, seems to us to be the crucial question for future research on the theme of self-healing as well as for its possible application to therapy.*

In our research endeavors we have thus far attempted to examine experimentally only two aspects of the vulnerability hypothesis: the detection of markers and the differences between recidivists and non-recidivists. We shall first deal with the question of recidivism.

**The study of recidivism**

We have been studying schizophrenic disorders among long-term outpatients of the Veterans Administration in the Pittsburgh, Pennsylvania area.** This is a prospective study of socioenvironmental factors associated with relapse in schizophrenia. The hospital outpatient population is screened for individuals under 56 years of age who meet the Research Diagnostic Criteria (RDC) (58) for schizophrenia and show no evidence of current alcohol or drug abuse. After a baseline assessment covering mental state and psychiatric history, as well as current social network, continuing difficulties, and selected aspects of premorbid functioning, patients are interviewed every four weeks for two years using a structured clinical instrument. A life event schedule is administered every twelve weeks, while changes in continuing difficulties and the patients’ social networks are assessed annually.

It is too early to give any definite indication of the trend in the findings of this study. Regarding the role of triggering life events, though two-thirds of the relapsed patients reported at least a single life event occurring in the three-week period prior to the appearance of positive psychotic symptoms, many of these events were not independent events but appeared to be provoked by the illness. Furthermore, several of the ‘triggering’ events seemed to be of an insignificant nature. Some of the patients reported several equally stressful events but relapse did not follow inevitably in each of them. It is likely that as the analysis of the data progresses it will become necessary to extend the triggering mechanism to include not only the dramatic life events but also the continuous sources of stresses offered by the noxious niches that some patients occupy. These daily hassles may produce stresses which tend to accumulate over time and finally reach a threshold of stress which triggers an episode. It will also be necessary to consider the moderating variables of premorbid personality and social networks which may serve as buffers against stress if they are positive or as exacerbators if they are negative.

In testing the tenability of the vulnerability hypothesis it would be well to utilize not only the veteran population which we are sampling but other populations as well. The veteran population under study is largely an older long-term sample with many individuals who do not have families. The results for such a sample might be

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* For further discussion of the role of natural healing see Zubin (57).
** This investigation was directed by Dr. Richard Day and F.R. Ayre.
quite different than for a sample of first episode individuals early in their illness. It is also likely that the latter might prove to be a more suitable sample for validating the general assumption of the model. It is likely that a long-term study of unaffected siblings of schizophrenic probands might provide answers to some of the questions that can not be answered by studying the probands themselves.

The search for markers of vulnerability

From the very beginning of our research in vulnerability (24, 44) it became clear that if vulnerability exists, it should be detectable not only in those who have expressed their vulnerability in an episode but even in those who had not developed phenotypic episodes of schizophrenia. To that end, the various measures which differentiated schizophrenics from normal subjects were scrutinized for their potential as markers of vulnerability. In order to be useful for detecting vulnerability, a marker should, according to Zubin et al. (54), have the following characteristics:

a. Be present premorbidly, morbidly and postmorbidly in probands with a frequency greater than in a suitable control group drawn from the general population.

b. Be present in siblings to an extent greater than in a comparable group of the general population.

c. Not be prodromal in character. If it is, it may be a consequence of the episode and hence would not be suitable for detecting the unaffected vulnerable individual or schizotropes.

d. Not be an episode marker which normalizes when the schizotrope emerges from his episode.

The results of this search have been presented in several papers (5, 20, 54, 59). Until the 1980s the search for the markers has been largely unsystematic, and thrived only on serendipity.

With the development of information processing studies in normal subjects, a baseline became available for noting where the schizotrope might deviate from normal expectancy. Since the 1980s the search has become more systematic as a result of adopting the information processing paradigm for pursuing the search (60–62). Psychophysiological measures are uniquely suited to this purpose because they provide a direct assessment of central nervous system activity accompanying information processing. Furthermore, since most of the responses to the tasks used in probing information processing occur within the first 1000 milliseconds following stimulation, it is likely that such laboratory tasks would not be influenced as much by life experience and past history as would tasks of longer duration that are more dependent on the influences of the environment. The psychophysiological markers that seem promising are (a) smooth pursuit eye movements; (b) event related potentials; (c) pupillography; (d) heart rate; (e) skin conductance and (f) blink rate. Schizophrenics and their relatives also have been shown to perform similarly on a series of behavioral techniques which tap information processing activities. The Continuous Performance Test and Span of Apprehension techniques, dichotic listening; reaction time, and visual backward masking are among the most notable. Little or no data are yet available on the distribution in first-degree relatives of pupillary dilation and cardiac responses, two of the measures which appear deviant in schizophrenics.
FUTURE OF VULNERABILITY RESEARCH

Thus far we have tackled only two aspects of the vulnerability model: the search for markers and the search for triggering mechanisms. We still need to deal with the other criteria for determining the tenability of the hypothesis: (a) the moderating variables that tend to either buffer or exacerbate the stress required to trigger an episode; (b) factors that terminate the episode; (c) factors leading to relapse; (d) factors determining whether schizophrenia is truly episodic; (e) the problem of chronicity.

What are the potential shortcomings and virtues of the vulnerability hypothesis?

It is, of course, possible that the vulnerability hypothesis may be tenable only for a subgroup of patients and not be applicable to other subgroups.

Among its potential shortcomings is the assumption that an episode is characterized primarily by positive symptoms which are usually time-limited to the episode. As for the negative symptoms the assumption is that they are largely non-indigenous to schizophrenia (63). By the same token, chronic schizophrenia which is largely characterized by negative symptoms is assumed to be largely artifactual (5). Only further research can resolve this issue.

Other shortcomings are the need to find patients who are drug free in order to eliminate the possible effect of neuroleptic treatment. The fact that non-affected relatives may show the markers even though they have not had episodes will help in identifying vulnerability markers. This would eliminate the possibility that the marker in question reflects the effect of episodes and is not to be taken for a vulnerability marker. There is always the possibility that a given marker may not be specific to schizophrenia. However, by examining the patterning of the markers it may become possible to find patterns that are pathognomonic to schizophrenia.

Among its potential virtues are that it provides for the interaction between the biological and environmental models of etiology. It tends to offer a more optimistic view of schizophrenia than the one afforded by the medical or biological model. One may wish to know how the vulnerability model differs from the prevalent medical model. The essential difference is that according to the medical model a person diagnosed as suffering from schizophrenia is essentially a sick person who for longer or shorter periods may appear to be well (in remission). According to the vulnerability model, the person is essentially well, and would remain so, were it not for the exigencies of living that induce stressors which elicit the vulnerability, producing longer or shorter episodes of illness. These episodes are not permanent, irreversible states, but disappear eventually though they may leave scarring.

If a group of markers become available, a program of prevention can be developed by studying the group of individuals who carry the markers (the schizotropes) but who do not develop episodes. Perhaps the factors protecting them will be revealed and steps can then be taken to protect the vulnerable individual through either educational or other preventive methods. Similarly, by studying recidivists and non-recidivists, factors preventing recidivism may emerge. In this fashion the threat that schizophrenia presents may be lessened and the burden it creates on the individual, his family, and society, reduced.
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