Vulnerability as a Model for Schizophrenia

Joseph Zubin

Biometrics Research Unit,
New York State Department of Mental Hygiene

Delivered before the New York Society of Clinical Psychologists, June 7, 1974, 8:30 P.M., Carnegie Endowment, 345 East 46th Street, New York, N.Y.

Introduction

It has been a long time since I addressed your society, almost 15 years, I believe, and many of you have entered the field since then and are probably wondering what you can learn from a biometrician. Much has happened during the last 15 years. Most of you who are past 50 can recall the days before the advent of the drug revolution when custodial care of mental patients was the mode, psychosurgery was in bloom, electroshock treatment (ECT) flourished, and insulin therapy was in flower. Those were heroic days, life seemed simpler; diagnosis was unnecessary, psychotherapy was in doubt, and psychoanalysis very rewarding, at least to analysts. Our hospitals were overcrowded, community psychiatry not even a pipe dream, and sensitivity training unheard of. The air was still clean, our language still pure, our noise level bearable, our youths still tractable, women still unliberated and our politics, pre-Watergate. With the advent of the drug era, all hell broke loose! The air became dirty, language foul, noise level unbearable, youth impossible, psychoanalysis declined, diagnosis again became necessary because our choice of therapies multiplied, our mental hospitals began to empty, and our entire environment and culture became threatened by pollution. Yet,
there seems to be a balance in nature -- a law of conservation of pollution -- for when our air, language and politics were clean, noise level low, and drugs were still medicine, sex was a dirty word, and now, with sex cleaned up, look at the mess we are in!

In addition to the revolutionary events that I have already described, two more movements developed. Because of the great demand and respect that developed for the mental health professions since World War II, some members of our profession, especially those of the psychiatric persuasion, assumed the mantle of omniscience and omnipotence towards all the ills of mankind extending their scope to improving the well as well as treating the ill. This movement has already given rise to a doggerel which runs something like this:

```
once
There was a doctor named Peck
Who fell in a well "on" his neck
His friends all agreed, he should have known
To treat the sick and leave the well alone.
```

This tendency to spread mental health work thinly beyond its capabilities has so outraged some otherwise sensible and persuasive men, that they launched a counter offensive declaring all professional work in mental health a conspiracy and mental illness itself a myth concocted to maintain the conspiracy. At the other end of the spectrum, a group of practitioners and researchers, impressed by the practical success of pharmacotherapy and by the theoretical success of genetic research in schizophrenia have begun to accept biology as the primary source of schizophrenia and to reject the environmental and psychotherapeutic aspects entirely.

I can not bring back the good old days of the pre-drug era, but I would like to take up the issue of the mythical nature of schizophrenia
on the one hand, and the self-imposed blinders on the other hand, of those who regard the biological approach of drugs and genetics as the only worthwhile approach to our problem.

Let me briefly dismiss the myth hypothesis first. Science as you know, deals with two components: facts and fictions. The facts are the ostensive observations that we can point to and assess, measure, and convert into data. The fictions are the concepts which hold the data together, for without such fictional concepts as gravity, magnetism, cancer, etc., we would have discrete observations without any meaning or significance. Therefore, about facts we can ask whether they are true or not, but about fictions we can ask only whether they are useful, and the moment they cease being useful we drop them. This has happened to phlogiston in chemistry, miasma in infectious diseases, the four humors in physiology and a variety of other concepts that have outlived their usefulness. In the course of this talk I hope to show that schizophrenia is still a useful concept, and worthy of continued interest.

As Kety recently pointed out, if schizophrenia is a myth, then it must be a myth with a heavy genetic loading. Furthermore, the fact that schizophrenia knows no cultural frontiers, occurring in all cultures, has been demonstrated in at least three recent international studies. The WHO has recently completed a nine-country study which sampled both underdeveloped and Western cultures, ranging from Nigeria to Russia to the U.S. and from India to the U.K. in which patients with profiles indicative of schizophrenia were found in each of the nine cultures. The U.S.-U.K. project has found similarly, patients with the same profiles in each of these two countries even though they were not always labeled
similarly by the indigenous clinicians, and our discussant, Dr. Katz has conducted cross-cultural studies in Hawaii in which schizophrenia was found in each of the subcultures, Japanese, Chinese and Hawaiian.

If it is a myth, it is a ubiquitous myth that apparently can not be 

\textit{exorcised} \textit{limbed} by fiat.

As for the biological-genetic thrust, I deal with it in the following way. Instead of accepting biology as the unique basic cause of schizophrenia, I am proposing a wider spectrum of potential causes which induce a vulnerability in a person, and that is why I am making vulnerability, regardless of cause, my chief text for tonight.

II. The Vulnerability Model for Schizophrenia

One of the most baffling problems that faces the schizophreniologist is the absence of any demonstrable aetiology for the disorder. We suffer from a paucity of proof in the midst of a plethora of possibilities and it has often been asked why when we are so smart in theory are we so poor in facts. When faced with such an impasse, the only solution is to develop each of the available theories to such a level that they generate hypotheses which can be tested for their tenability. The untestable theories will be left to fade away or to slowly twist in the wind.

Some of the approaches which have not yet succeeded in developing empirically testable hypotheses are psychoanalysis and existentialism which, though they have given us many insights, have not yet provided a framework for experimental verification of their tenability and perhaps never will. It is true that experimental verification through measurement is not the only road to knowledge, but it is the only public road which others can also traverse. Otherwise it remains a private road which only
the existentialist or the psychoanalyst and their chosen disciples can traverse. Two brief examples of puny unsuccessful attempts at testing psychoanalytic principles might amuse if not enlighten you. (Story of headache and story of the Oedipus situation.)

The process of subjecting a conceptual framework to empirical verification usually takes the path of building a scientific model composed of a parsimonious number of dimensions from which specific testable hypotheses can be drawn. I need not go into any proof that scientific models are necessary for this audience, but if anyone needs proof, he might find it in the following excerpt of a sonnet:

"Upon this gifted age, in its dark hour,
Rains from the sky a meteoric shower
Of facts ... they lie unquestioned, uncombined.
Wisdom enough to leech us of all our ills
Is daily spun; but there exists no loom
To weave it into fabric..."

Edna St. Vincent Millay -- Collected Sonnets

The scientific model is an attempt to provide the loom for weaving the wisdom into fabric.

In an attempt to apply such a procedure to the field of schizophrenia, the first obstacle one meets is the definition of the disorder. Historically, schizophrenic-like behavior has been noted in mankind for at least 3½ centuries. Only recently, however, has it become possible to crystal-

lize the phenomenology transmitted across the centuries into empirically observable bases for classification. With the help of systematic structured interviews covering the entire waterfront of psychopathology
it has become possible to develop an anatomy of psychopathology consisting of a finite number of dimensions which present a profile of the individual patient in a reliable way. (Slides of items of PSS only, but briefly discuss others.) Secondly, with the help of specified criteria in a glossary, it can be empirically determined whether a given profile meets the criteria for schizophrenia. (SLIDE of criteria for non-affective schizophrenia, indicate criteria for schizo-affective manic and schizo-affective depressed.) To be sure, these criteria are arbitrarily chosen by fiat from a larger group of criteria that have been in vogue over the years, but without such an operational definition, we could never be sure that we are dealing with similar patients. fn

Thus, armed with a profile and with criteria for classifying the profile into relatively homogeneous categories, we can proceed to examine the other common denominators that characterize schizophrenics beyond the profile, and in this way perhaps unravel its etiology and determine on its therapy. In the process, we may discover that the hoped for homogeneity was a delusion and that the group we call schizophrenia is itself made up of a variety of subgroups, but this is exactly what happened in the

fn It should be realized that arbitrary definitions for operational purposes is the vague rather than the exception in the life sciences. Only in mathematics can we entertain rigorous definitions that bear no exception. In biology, even such a useful fundamental concept as 'species' can not be defined rigorously. Julian Huxley (1940) points out that ... "there is no single criterion of species. Morphological differences; failure to interbreed; infertility of offspring; ecological, geographical, or genetical distinctions — all those must be taken into account, but none of them singly is decisive ... A combination of criteria is needed, together with some sort of flair."
investigation of other disorders both physical and mental, and would be additional evidence of the essential validity of our approach.

The model for the etiology of schizophrenia which I would like to present to you is that of a disorder occurring in an individual who is in a state of high vulnerability. I shall outline its assumptions briefly, and then expand on their implications for testing the hypotheses they lead to. The assumptions are as follows:

1. Vulnerability to stress-producing stressors leading to a schizophrenic episode is distributed normally in the general population. This vulnerability may be likened to vulnerability to an electric shock. Given sufficient voltage, every one will go into a convulsion though some may require more voltage than others, and some may not recover as readily and some may suffer residual effects and some even die.

2. If the stressors produce a degree of stress above the threshold of containment, the individual will develop an episode.

3. The episode is time limited.

4. When the episode ends the patient returns to his pre-episode or premorbid state, and can be regarded as recovered from the episode under examination.

Why then do some patients develop into chronic states? To answer this question we must take a detour into prognosis of schizophrenia. One of the most clearcut findings in prognosis of schizophrenia is that the patients with a good premorbid personality tend to recover while those with a poor premorbid personality fail to do so.

One explanation of this finding has been that the good premorbids are reactive schizophrenics and have a different disorder from the poor
premorbid who develop process schizophrenia. This, however, introduces a non-parsimonious distinction which may not be necessary. Furthermore, attempts at differentiating good and poor premorbid on the basis of other criteria often failed to establish the distinctness of these two categories. Another explanation of this finding is that, following our model, the episode of schizophrenia ends in both good and poor premorbid patients similarly. In the case of the good premorbid, once the episode is over, he returns to his pre-episode status and resumes his place in society more or less at about the same level he had before the episode. The poor premorbid also resumes his pre-episode level, but since he could not cope adequately with life's exigencies before the episode occurred, the end of the episode is hardly noticeable in his case. Furthermore, the regimented milieu of the hospital or other treatment facility may provide him with a protective environment which he can learn to cope with, and which he can not find on the outside. Any attempt to release him may arouse his anxieties to the point where he may either appear still ill, or may in the process develop still another episode. He may also find certain symptoms sufficiently rewarding to retain them either consciously or unconsciously and in this way acquire permanently a repertoire of iatrogenic chronic behavior designated by Gruenberg as the Social Breakdown Syndrome. This, in brief, is the model of vulnerability that I want to place before you.

Let us now examine more critically some of the terms used in this model. The concept of vulnerability itself merely indicates that individuals differ in the degree of stress that they can withstand before succumbing. It is really a threshold phenomenon as shown in Graph l.
It will be noted in Graph 1 that as long as the stress is below the threshold of vulnerability, the individual remains well, responding to the stressor in an elastic, homeostatic way, within the bounds of normality. When the stress goes above the threshold line, the person develops an episode, but as soon as the stress recedes below the threshold line, the episode ends and the person begins to return to his pre-episode level. There may be a small proportion of the population who appear to be incapable of dealing with the normal stresses in their ecological niche even when no added stress is introduced and appear to be suffering a continuing episode. Such individuals, in response to increased stress may go into a more marked episode, but upon their recovery from the additional stress will still appear as if their episode is continuing because of their high insensitivity in everyday events prior to the episode.

One paradigm for the vulnerability-stress model is Hooke's Law which states that when the load of a weight is applied to a string, a stress will ensue within the molecules composing the string, producing a strain which extends the length of the string, \( l \), by the amount \( \Delta l \) and \( \Delta l / l \) can be taken as a measure of the strain. This strain is physically a measure of the presumed stress, since in physics, action and reaction are equal. Once the load is removed, the string if its elasticity has not been exceeded, will return to its former length, \( l \), or, if the load exceeded its elasticity a permanent dislocation of the molecules has extended \( l \) to a new length \( l + \Delta l \). In some cases, the load may be so heavy that it will cause a complete break of the string.

Applying this model to schizophrenia, the weight imposed on the strin
corresponds to the stressors impinging on the individual. The degree of
elasticity of the string corresponds to the vulnerability of the
individual. The strain, as measured by the elongation of the string
corresponds to the alteration in behavior produced. Unfortunately, unlike
the physical case, in psychopathology we can not yet measure the internal
stress by the outwardsly appearing strain (behavioral change), because we
have no good measures of total strain yet. According to our vulnerability
model, we had assumed that the episode of schizophrenia usually recedes
and leaves the person approximately in the same state as before the
episode overtook him. It is, however, possible, that in the case of some
individuals, the episode may leave a lasting residual effect (like the
extension of the string by $\Delta l$) or that in the case of others, it may
actually disrupt him completely, bringing on catastrophic deterioration,
(broken string in the Hooke's Law model). However, according to most
recent findings, (Manfred Bleuler, for example) the number of such patients
is very small, and whatever residual effects persist may be iatrogenic
rather than a necessary sequel to the episode. According to Manfred
Bleuler's follow-up of 200 schizophrenic patients for 20 years, from the
cohort admitted to the Burghölzli Hospital from 1941-1962, catastrophic
schizophrenia (acute onset followed by immediate deterioration) is dying
out and becoming increasingly rare, not a single case being observed by
him in his follow-up, though his father had noted from 5 to 18 per cent
in this category in earlier cohorts. About fifty per cent of Manfred
Bleuler's probands were able to live independently in the community and
earn their own living and only twenty-two per cent were under care in a
mental hospital. Thus, nearly eighty per cent of the cohort seemed to
be in the improved category not requiring hospitalization.
III. Causes of Vulnerability

Thus far, our discussion has been somewhat circular. We have pointed out that individuals who develop a schizophrenic episode possess a highly vulnerable diathesis. But what is this vulnerability due to?

In searching for the etiology of the mental disorders which underlie the vulnerability the following approaches have been suggested: (1) ecological; (2) developmental; (3) learning; (4) hereditary; (5) internal environment, and (6) neurophysiological.

The ecological approach postulates that the sources of schizophrenia are to be sought in the parameters of the ecological niche which a person occupies. Among the parameters that have been proposed as causes of mental disorder are (1) low socioeconomic status, (2) degree of disorganization present in the social milieu, (3) degree of crowding, (4) minority status in the community and a host of similar variables. Unfortunately, the taxonomy of the parameters of the niche influential in good as well as bad health is not yet available and the infinite number of such parameters makes systematic studies well nigh impossible. Cassel (1974 -- American Handbook of Psychiatry, Second edition) has pointed out that throughout history certain environmental factors have been implicated in the cause of disorders, but the specific factors have varied considerably over time from "airs, waters, places" of Hippocratic times to the microchemicals and microorganisms of today. Factors selected for study reflected the etiological theories of the day as well as the existing level of technology. Reflections of these tendencies persist in such terms as malaria (bad air), hysteria (wandering uterus), melancholia (black bile) etc. Because it is impossible to do controlled experimental studies on man's ecology, animal studies have been resorted to. Among the findings are that one of the most
important factor in the environment is the presence of other members of the same species. Thus, overcrowding among strangers takes a totally different toll than the same degree of overcrowding among familiar peers. The link between population density and high risk of disorder is not mere propinquity but the disorganized social relationships between individuals that ensues and these depend in turn on (1) the importance or salience of the relationship that becomes disordered (mating, rearing of offspring), (2) the position of the individual experiencing the disordered relationship in the status hierarchy, (3) the degree of previous experiences with such disorganization, and (4) nature and strength of the available group support.

Whether the constantly present chronic stresses that characterize a given niche are capable of producing an episode, or whether a downward (or even upward) shift in the parameters of the niche -- a crisis -- is required for an episode to occur is still a moot question.

Thus, individuals may develop an episode in response to their ever present stress even when no change in stressors occurs, or they may become habituated to a continuing stressful situation and tolerate it without developing an episode, and only when a change in stress occurs will an episode develop.

The evidence from immigration and migration statistics for hospital admissions would incline us to believe that change in stress is the important factor while the rate of schizophrenia in low socioeconomic niches might incline us to believe that constant continuing stress is sufficient. The Dohrenwends ( ) have proposed a crucial test of this question by examining data for schizophrenia in old Americans and new Americans found in the various socioeconomic strata. If the stress produced by change in a niche
is the effective producer of schizophrenia, then the newly arrived Americans who have reached the upper socioeconomic levels should have the higher rates, since they have undergone more changing stress. If continuous exposure to the same noxious stresses is the cause, then low socioeconomic status old Americans who have occupied their present niche continuously should have the higher rates. The reason for this is, that the newly arrived Americans in the low socioeconomic status consist of two groups, those of low vulnerability who have not yet managed to climb upwardly and because of their low vulnerability are immune to the stressors of their noxious niche, and those of high vulnerability who may succumb. The presence of the low vulnerability group would dilute the rate and lower it. The old Americans of low socioeconomic status are largely of the highly vulnerable type, since the low vulnerables have moved upward in the general thrust for upward mobility in the population, letting the highly vulnerable sink to the bottom.

The developmental model postulates that the cause of schizophrenia is to be sought in the transitional phases of the developing individual as he develops from fertilized ovum to embryo, foetus, neonate, child, adolescent, adult, senior citizen etc. The particular nourishment, supplies, reinforcements necessary for him to pass from one stage to the next are the critical elements in maldevelopment. Thus, if the placental nourishment is insufficient for the embryo, if the intrauterine environment is noxious for the foetus, if early mothering is inadequate for the neonate, if family organization is defective for the child, if peer group relationships are deleterious for the adolescent etc., trouble may be expected in so far as it renders the individual more vulnerable to life exigencies. Whether these
noxious events are sufficient to produce schizophrenia on their own account has not been demonstrated but they may be necessary if not sufficient causes.

The learning theory model stipulates that schizophrenic behavior develops through learning just as normal adaptive behavior does. Essentially, schizophrenia consists of a complex of deviant behaviors that have developed as a result of life experiences which have rendered the individual more vulnerable to future stresses.

In searching for the learned or acquired sources of vulnerability following the learning theory model we must first specify the observable deviant behavior which the schizophrenic exhibits, determine the occasions in which they are exhibited (the S's or discriminative stimuli) and determine the reinforcing contingencies which tend to maintain it. Once these three components are determined, therapeutic intervention can be utilized for eliminating the deviant behaviors through behavior modification techniques. It is interesting that behavioral analysis includes within its scope a diagnostic component as a prerequisite for determining what therapeutic intervention is required, and behavioral analysis bids well to become a competing diagnostic system against the current nosology.

The hereditary model assumes that the determining component of schizophrenia is an inherited propensity without which the disorder could never occur and that this is the basis of the vulnerability characterizing a person. It is perhaps the most highly developed model of vulnerability we now have available and has far outstripped the other models quantitatively if not qualitatively. Recent developments have permitted crucial contrasts between the relative importance of rearing versus genes in the transmission of schizophrenia through the comparison of the biological and adopted relatives
of probands who were born to schizophrenic parents, but were adopted early in life. The role of heredity appears to be far stronger than that of environment but this gain is bought at some sacrifice since the concept of a schizophrenic disorder has to be broadened to include a wide spectrum including milder instances of schizophrenia-like characteristics. Unfortunately, we have no measures of environmental similarity as objective as those for genetic similarity, and this may be the reason why the measured genetic factor appears the stronger. When better measures of the environment become available a better assessment of the contribution of the environment to schizophrenia will become possible.

The internal environment model postulates that the roots of the disorder are to be sought in man's biochemical metabolism, body fluids and body chemistry. The first attempts implicated peripheral metabolic correlates circulating in the bloodstream such as adrenochrome, taraxin, and all the body fluids were subjected to a critical inspection to find the noxious agent, but it was not until central synaptic mechanisms became the focus of attention that progress began to be made. Two hypotheses explaining vulnerability are now in the ascendency: excessive transmethylation and disturbance in catecholamine synapses. Methionine is a substance which favors transmethylation and when it is administered it exacerbates psychotic behavior in a significant proportion of schizophrenics, but produced no effect in normals. Amphetamine which produces a psychosis resembling paranoid schizophrenia also releases dopamine at catecholamine-containing nerve endings. Since phenothiazines produce a blockade of dopamine receptors in the brain and also alleviate the psychosis, it is postulated that excessive amounts of dopamine lie at the root of the vulnerability to schizophrenia, and for this reason it becomes possible to reduce the
psychosis by blocking dopamine. Apparently, this interference with
dopamine eventually produces parkinsonism and
L-Dopa is required to alleviate it.

A genetic marker for schizophrenia has recently been reported in the
discovery that monoamine oxidase is markedly reduced in the platelets of
schizophrenics and is found to be present in both the affected and non-
affected members of discordant pairs of monozygotic twins.

The neuropsychiological model postulates that the vulnerability of the
schizophrenic is to be sought in the processing of information in the
central nervous system of the schizophrenic. For the last 100 years it had
been assumed that the sensorium of the schizophrenic was sound while his
mind was unsound. More recently evidence has been accruing that the sensory
functioning of the schizophrenic is not the same as that of the normal.
Perceptual and cognitive tests have always found schizophrenics to be
defective in performance but such deviation could be easily attributed to
lack of motivation or interest or effort. As our laboratory techniques
became more sophisticated, the difference between schizophrenics and normals
in these complex tasks diminished when controls for poor motivation and
effort were introduced.

With the introduction of forced choice methods and signal detection
theory in which sensitivity is separated from criterion (attitude,
unwillingness to take a chance etc.), it became apparent that many of the
erlier findings such as higher threshold for critical flicker fusion were
due to differences not in sensitivity but in caution. In order to eliminate
such criterial differences we sought for tasks in which the schizophrenic
would excel the normal. We have found several such techniques but I have
time to tell you only about two of them: (1) energy integration and
(2) auditory masking. We began with the Bunsen-Roscoe Law which states that up to a certain critical duration of the stimulus (13 milliseconds in our particular apparatus) you can exchange time with intensity and leave the response unaltered as long as the total energy of the package remains constant. To our great surprise we found that this critical period was much shorter in schizophrenics. They detected a difference between 4 and 6 milliseconds which the normals failed to react to. This kind of a performance can hardly be blamed on lack of motivation. The second technique in which the schizophrenics excel is an auditory masking experiment in which a click, 25 decibels above threshold, is followed 15 milliseconds later by a 10 decibel click. Our patients decrease their reaction time to this pattern of stimulation compared to the 25 decibel click alone while the normals fail to do so. An examination of the dimension of psychopathology which characterizes these patients indicated that they were primarily suffering from manic depressive psychosis and differed from schizophrenics who were essentially normal in their performance. The energy integration task mentioned earlier characterizes the schizophrenics who suffered from thought disorder, but no other schizophrenics or other mentally ill patients.

After reviewing these etiological models one is left with the feeling that there must be a common denominator running through all of them. If you were to squeeze out their juices into a goblet, you would probably find that the essence of the resulting elixir is vulnerability no matter how it arises. It should also be realized that none of these models works in isolation. There is always an interaction between all of them, though the ingredients may vary from one disorder to another. Thus, it is quite possible
that for schizophrenia, a higher loading will appear for the genetic component than is the case for neurosis, and that for depression, a higher loading will appear for the internal environment than would be the case for character disorders.

A rather unusual aspect of this interaction is provided by the studies in nutrition. Stephen Zamenhof (UCLA - ?) has recently shown that "when an underfed female rat was mated with a well-fed male, the resulting newborns showed distinct signs of brain malnutrition -- as expected -- even though they were put on an adequate diet starting at birth. The surprise came when the offspring, the second generation of females, which had been well nourished throughout their lives and during their own pregnancies, nevertheless gave birth to newborns with brain growth likewise retarded. The mothers were apparently unable to develop a placenta adequate to the proper nutrition of the fetus. Thus, in the case of these rats, at least, the curse of malnutrition was carried into the third generation."

[Rosenfeld, A., (Science Editor) Starve the child, famish the future. Saturday Review World, 3/23/74, p. 59.]

A similar effect is found in the treatment of their own first offspring in Harlow's monkeys who were raised with surrogate mothers and without peers. Apparently in addition to the simultaneous interaction of the various etiological models, there may also be interactions stretching backward in time.

How many subsequent generations may be handicapped by the malnutrition, deprivation, and other insults suffered by their progenitors is a moot question, but to attribute the possible effects of malnutrition and other environmental insults to genetic inferiority is indeed adding insult to injury.
IV. Detection, Description and Diagnosis of Vulnerability

Let us now turn our attention to the detection, description and
diagnosis of vulnerability and its assessment in some quantitative manner.

It is obvious that at this point in time, we have no way of detecting
directly the presence of vulnerability nor of measuring it. We can,
however, by making certain assumptions based on our scientific models,
select populations which presumably vary in degree of vulnerability. Thus,
if we accept the ecological model, we would expect the occupants of noxious
ecological niches to be more vulnerable than those of more favorable niches.
If we adopt the developmental model, we would expect that children whose
mothers underwent severe toxemias of pregnancy or birth trauma, adolescent
deprived of satisfactory peer groups, students frustrated by lack of
opportunities would be highly vulnerable.

Similarly, the learning theory model would lead us to expect that
children growing up in disorganized families, or individuals who have
developed low self-regard because of continued failure, would be highly
vulnerable to life event stresses. The internal environment would lead us
to believe that individuals who possess certain biochemical anomalies
would be vulnerable while the neurophysiological model would lead us to
expect that individuals who show certain psychophysical and neurophysio-
logical anomalies would be prone to schizophrenia.

One obvious approach has been pioneered by Weston and by Mednick in
the selection of high risk populations genetically. Under the assumption
that the genetic component is important in the development of schizophrenia
it follows that the offspring of schizophrenic parents should have a higher
risk of developing schizophrenia than the offspring of parents free of
schizophrenia. This indeed is the case, with the offspring of one
schizophrenic parent having a risk of fifteen per cent of developing schizophrenia (10 - 15 times as high as in the offspring of normals) while the risk for offspring of parents both of whom are schizophrenic rises to forty per cent. This approach presents us with populations of graded risk which could yield significant information regarding the interaction of the genetic with the other etiological models.

Unfortunately, the other models have not yet provided us with measures of vulnerability as good as those which genetics is equipped with in blood-relatedness. In this respect, the social scientists, developmentalists, behavior theorists, biochemists and neurophysiologists have failed psychopathology.

There is some indication that the ecological model which has thus far looked to SES measures as indicators of vulnerability may instead provide measures of vulnerability by studying the life-events that occur in the niche the person occupies. The degree of readjustment a given life event elicits may give an indication of the degree of vulnerability.

A combination of ecological, developmental and learning considerations may perhaps yield a measure of vulnerability which might be comparable in value or even greater in value than the vulnerability measure provided by graded genetic blood-relatedness to schizophrenic probands. If we develop good measures of premorbid personality following the developmental stages of the person, and if we determine by a study of the premorbid history of the patient, the life-events to which he reacts with greater stress, we might be able to develop a measure of vulnerability titrated against personality characteristics and against the significance of life events which are perceived as stressful. Thus, if we determine the type of personality the patient possesses, the kind of event contingencies which are stressful to him, we might be able to develop a scale of vulnerability
that could become useful for effective intervention.

As for the internal environment, the presence of monoamine oxidase in the platelets of the blood, the measurement of the various neurochemical transmitters, and the variety of other biochemical indicators might eventually yield a vulnerability indicator.

As far as the neurophysiological model is concerned, measures of energy integration, auditory threshold and masking studies, reaction time, pupillography and evoked potential studies have yielded sufficient differentials between schizophrenics and other mentally ill and normals which could constitute a basis for a tentative vulnerability scale. The developmental model may develop a longitudinal measure of ease of transition from one stage to the next which the subject exhibits which may give an indication of vulnerability: The learning theorist may develop measures of tolerance for aversive stimulation. A combination of all of these scales may yield an index of vulnerability which can then be instrumental in successful intervention. Perhaps the time has come to develop such an instrument, encompassing what we have gained from all the varied approaches to the etiology of schizophrenia.

V. Relation of Vulnerability to Therapeutic Intervention

Having developed a means of selecting populations of varying degrees of vulnerability, and a tentative measure of vulnerability we can now proceed to discuss the relation of vulnerability to therapeutic intervention. The important aspects of therapeutic intervention is to know when to intervene, how to intervene, what the goal of intervention is and how to evaluate its efficacy. We have to confess at the very start that the information required for answering these questions is non-existent. When to intervene is of course, often determined by contingencies beyond the therapists' control. Rarely does the therapist have sufficient control
of the situation to intervene at the most critical point in the course of
the episode, even if he knew which it was. The patient may come at such
an advanced stage that the critical point for intervention is passed. Nor
do we know which is the best therapy for a given patient, though we can
determine which would be expected to be the best in the light of any
particular etiological model to which we might subscribe, as will be shown
later.

With regard to the goals of therapeutic intervention, an interesting
dilemma arises. Should we aim to cure the patient, return him to his
pre-episode level namely to his premorbid state, should we try to improve
on his premorbid state, or should we have a more modest aim of eliminating
the most painful symptoms and thus alleviate the condition sufficiently to
return him to his functioning capacity. These are questions which require
considerable thought. In any event, an assessment of the premorbid level
of the patient is a necessary baseline on which to build. Unfortunately,
most diagnosticians are chiefly concerned with psychopathology and dis-
regard the assessment of personality with its assets as well as its liabilities.

What is the relation between personality and psychopathology? Else-
where (Zubin ) I have pointed out that personality and psycho-
pathology may be essentially the same, the personality of the schizophrenic
consisting of his psychopathology, and his psychopathology consisting
essentially of his personality, a view which Freud might have subscribed
to. On the other hand, personality may represent systematic behavior inde-
pendent of psychopathology as Kraepelin might have said, since schizophrenia
is a disorder which could occur in any type of individual, just as many physi-
cal disorders may be independent of personality. The third possibil-
that of interaction between the two, i.e., that psychopathology tends to divert the personality from developing wholesome even as a blight disturbs the growth of a plant, a view which Adolf Meyer might have espoused. Until recently, the weight of the evidence seemed to make each of these possibilities equally tenable. Essen-Möller and his student Ølle Hagnell, however, have recently demonstrated by applying the Sjöbring method of personality evaluation to their "Lundby" population of some 2600 individuals, that the premorbid personality was independent of subsequent psychopathology, although once an episode developed it was colored by the premorbid personality. They reached this conclusion because the individuals whom they tested in 1937 and who were found to be free of psychopathology, but who developed an episode of mental illness during the succeeding ten years, had, in 1937, personalities that did not differentiate them from the rest of the normal population. Another finding, tangential to schizophrenia, is the fact that of 22 women who belonged to one Sjöbring personality category, 20 developed cancer during the 10 year follow-up period. For these two reasons, we have attempted with the help of Professor C. Eberhard Nyman of Lund, Sweden (one of Sjöbring's students) and Dr. James Barrett of the Eric Lindemann Center in Boston, to develop a systematic structured interview based on the Sjöbring method to assess personality.

If we could have access to individuals in their premorbid state, as might be the case when we examine a high risk population, it might be well to determine from their personality characteristics what particular aspects of their behavior might benefit from intervention. If we base our intervention on the ecological model we would try to modify the environmental surround sufficiently to prevent any of the noxious forces of the ecological
niche from producing the degree of stress necessary to cross the threshold of vulnerability. Unfortunately, we do not yet have a taxonomy of the parameters of the environment to make such intervention satisfactory. Cassel has maintained that if he could obtain sufficient funds he could reduce the high rate of schizophrenia in the county of South Carolina where he did his studies to a level well below the prevailing rate and even below the rest of the country. He regarded poverty and its accompanying features of malnutrition, social disorganization, lack of proper training and vocational guidance as the primary source of schizophrenia as well as of suicide and TB which were also rampant in his country.

If we accept the developmental model, we would take to heart some of the findings regarding the role of adolescent friendship patterns and precocious maturity in the development of schizophrenia. Dolores Kreisman has found that adolescents who subsequently become schizophrenic tend to lack intimacy in their friendships. Whether this is cause or effect of schizophrenia is still moot, but attempts at providing better friendship roles might be worth a trial in the hope of preventing the episode. Louise Cureton found that the one single common denominator characterizing the wayward adolescent youth she studied was the presence of a precocious physical maturity. Guidance and counselling of adolescents whose physical maturity runs ahead of their social-emotional development might avoid some of the unfortunate developments in such cases. Prevention of toxemias of pregnancy and birth traumas might reduce the risk of developing schizophrenia as might intervention at the other transitional stages in man's development. The great proportion of unmarried in the schizophrenic group offers a challenge of determining whether intervention might not make some of the vulnerable more amenable to marriage and thus offer another buffer against vulnerability.
If we accept the learning theory model, the entire armamentarium of behavior modification becomes available for possible prevention. If we get a developmental history of the personality development of a patient and of the life events that have proved stressful in the past, and of the contingencies which maintain his deviant responses, behavioral modification techniques could be instituted to eliminate or prevent them. A follow-up of Project Talent students (ref. through the files of the New York State Department of Mental Hygiene has indicated that certain test scores in high school are predictive of eventual hospitalization. Among these is a factor of verbal ability in which underclassmen (grades 10 and 11) who later become psychiatric casualties do less well than their classmates, while upper classmen who subsequently become casualties do better than their peers. All of the subsequent casualties do poorly on a reasoning factor and on an impulsivity factor.

Accepting the genetic model, genetic counselling regarding mate selection and offspring, might help prevent undesirable consequences.

These are mere suggestions of how we might intervene with premorbid personality development to help in prevention of developing episodes. As our knowledge of the internal environment progresses certain preventive psychopharmacological interventions might be resorted to. If we adopt the neurophysiological model, we might try to eliminate some of the differences that characterize the premorbid schizophrenic -- speed up reaction time, lower the auditory threshold through conditioning approaches and similar therapeutic interventions. Essentially, preventive efforts should be undertaken to obviate the development of schizophrenia as far as that proves possible.
With regard to the morbid state, once the episode has begun, attempts to contain it, to mitigate it and hasten its end are the desiderata. But the cure of the patient is not the total goal at least as far as the poor premorbid personalities are concerned. In their case, some attempt must be made to utilize whatever means we have at our disposal, be they behavioral or biochemical, to improve the coping capacity of the patient so that when the episode ends, he will be able to cope better with life exigencies. As for the good premorbid, who now occupy most of our therapeutic efforts, they might be largely left alone to attain their spontaneous cure, which will come with the ending of the episode, and spend most of our efforts on the poor premorbid who are in greatest need of improvement. Perhaps a careful study of the few poor premorbid who succeed and the few good premorbid who fail would give us indications of the underlying factors in success and failure.

As for the post morbid period, careful follow-up with an ever watchful counsellor might be necessary at least in the early stages of the post-morbid period. Here again, a carefully designed follow-up study of a sample of good and poor premorbid would yield the information required for improving therapeutic intervention. One principle that we need to recognize is that therapeutic intervention is merely a process for permitting the natural curative powers of nature to proceed without interference. What the good therapist does is to run interference for the patient against the hazards of life's vicissitudes.

VI. Summary

My purpose was to place before you a model for schizophrenia based on the hypothesis that vulnerability of man to stressful situations in his
life events is the essential factor in the development of a time limited episode of schizophrenia. Whether this holds true for all of schizophrenia is debatable, but it certainly holds true of the majority of schizophrenics. The causes of this vulnerability is still unknown but certain etiological models have provided some indication of what are the necessary though not sufficient causes of high vulnerability. Among these are genetic, ecological, developmental, learning, neurochemical and neurophysiological causes. A threshold curve was drawn connecting the perceived stress of life events and vulnerability, so that as long as the degree of stress remains below threshold, the person remains well; when the stress exceeds the threshold, an episode occurs, and when the stress recedes below the threshold, the episode ends and the individual returns in most cases to his pre-episode level of functioning. If this level was good, the patient returns to his place in society, if it was poor, the patient also returns to his pre-episode level, but since he could not cope premorbidly, it is hardly to be expected that experiencing an episode will improve his ability to cope with life's exigencies.

What role can clinical psychology play in diagnosis and therapeutic intervention, if this model is adhered to? Regarding the underlying biological causes of this vulnerability -- the genetic, neurochemical and neurophysiological substrate -- clinical psychology can do but little, except to learn to recognize them, appreciate them, and receive guidance in how to contain them. Regarding the other underlying causes of this vulnerability -- ecological, developmental and learning -- clinical psychology can play a leading role.
Clinical psychology with its interest in personality and in learning theory, developmental theory, ecology and psychometrics should be able to develop measures of vulnerability and measures of life event stresses so that the premorbid personality and life experience of the individual can be assessed objectively and reliably. Once this is known, therapeutic intervention based on behavior modification ought to help the poor premorbid to develop strategies of living so that the hazards of developing future episodes can be reduced. This is a task which clinical psychology is eminently suited for, and to quote Mordecai's warning to Esther when he entreated her to intervene with the King in behalf of her people:

"For if thou altogether holdest thy peace at this time, then will relief and deliverance arise to the Jews from another place, but thou and thy father's house will perish; and who knoweth whether thou art not come to royal estate for such a time as this?" (Esther, chapter 4, verse 14)

The vulnerable are waiting for us to pick up the challenge. Are we ready to take it?