INTRODUCTION

The invitation to the symposia which have been conducted by the Department of Psychology at Texas Tec states: "The guiding principle of these symposia is the focus on the need for greater interface between specialty areas within psychology." In carrying out this mandate it is interesting to note that the first symposium which was on Developmental Psychology and Clinical Neuropsychology was limited as far as I could tell - I did not see the program - to presentations by psychologists. The second symposium on Social Perception in Clinical and Counseling Psychology was also limited to psychologists' contributions although there was a contribution from the Institute of Social Research of Michigan. The third symposium on Cardiovascular Disease and Behavior, broke the mold and included two MD's. Our present symposium followed this pattern by also inviting two MD's. It is clear that the Department of Psychology at Texas Tec has begun to realize that the cutting edge of science knows no disciplinary boundaries. As is well known, the turning points in the development of science occur at the interdisciplinary crossroads. The father of modern psychology, Wundt, is the exemplar for this trend, by introducing physiology into psychology. I do hope however, that in future symposia there will be an opportunity to utilize contributions from sociology, anthropology, linguistics and other social and biological fields since psychology can benefit much from interaction with all the sciences.
Why is it that there is a need for cross-disciplinary interaction especially in psychopathology. In 1952 when I became interested in the application of scientific models to psychopathology I wrote an article on the "Powers of Models" and pointed out that as one continues his research in psychology, or in any other field, for that matter, one eventually comes to the border of the field and begins to note the greener grass in the neighboring fields. The temptation is great to borrow some of the concepts from the neighbors and even though they may not be used in the same restricted rigid manner that is customary in the field from which they are borrowed, one finds that his own field benefits. The field which lent the concept soon becomes interested and it in turn borrows from the borrower. It probably was in this fashion that biochemistry and other hyphenated sciences were born. In our symposium, the term stress, first objectified in physics and engineering with Hooke's modulus and measures of strain has moved into physiology and immunology providing us with at least tentative measure of psychological aspects of stress. To be sure, the psychological concept of stress involving the subjective feelings accompanying it can not be totally measured by physics, physiology or immunology. However, we must provide a public mirror for the private event and only by utilizing the objective measures provided by the other fields can we approximate the psychological concept.

Thus Kurt Salzinger while searching for a measure of flatness of affect hit upon the reinforcement of effective utterances as a potential measure for flatness of affect. While it is a far cry from how the clinician assesses flatness of affect, the index provided by the response to reinforcement was equally predictive of outcome with the clinical measures, but did not depend upon the unspecified clinical means for assessing it.

The question is often raised about the lag between measurement in psychopathology and measurement in other fields of science, especially the physical sciences. We regard evaluation in psychopathology as still highly intuitive, subjective and hence largely unreliable and invalid. But all measurement has to begin this way and in a sense psychology is the unfilled in which all measurement begins. The first measures of length, weight, time, temperature, and touch were originally subjective, self-referred and intuitively based. Let us look at the measurement of subjective warmth. Since there is no documentary evidence for man's initial attempts as gauging the cause and degree of subjective warmth, we shall resort to fantasy. Come with me to a cave in some prehistoric ice age, before fire was invented, and listen to a symposium on the origin of subjective warmth feelings. One savant declares that warmth depends on the number of skins covering the body. Another claims that it depends on duration of exposure to the sun. A third postulates swift running as the source of warmth and the distance covered as a measure. The medicine man in their midst raises a controversy because of his claim that his
patients often report and feel warm without the benefit of any of the other factors mentioned. The symposium ends without a resolution. But Prometheus later invents fire and it becomes possible to demonstrate that by adding fig-gots to the fire, subjective warmth is raised in all the inhabitants of the cave and by the same token removal of figgots reduces it. The first breakthrough has occurred. Man can manipulate an external agent to raise and lower subjective warmth at will. But this is still far from measurement. The first known historical breakthrough occurs in Egypt, where after the linguistic development of ratings in the grammatical form of positive comparative and superlative adjectives, rating scales are developed for measuring warmth in four steps—with warmth anchored at one extreme to the hottest day of summer, and at the other extreme to the coldest day of winter. Eventually, the expansion of mercury with increase of subjective warmth is noted, and the thermometer is born, and finally, humidity and air pressure are recognized as important factors, and the present-day discomfort index emerges. What were the essential steps in the process? First, the discovery of means of inducing changes in a subjective experience by external control. Second, the development of an external criterion for measurement independent of the self-referred subjective experience. The same process, no doubt, held true of the other measures which have attained great objectivity. Pain is still a subjective phenomenon without an external criterion, and without measurable ways of inducing it though recent efforts along these lines show considerable promise. Intelligence tests became objective when mental age scales were substituted for teachers' subjective impressions. Anxiety, depression, elation are still in the rating stage. In my fantasy, I sometimes imagine that we may find a life-bearing planet, somewhere in space, where anxiety has already been measured, but where warmth or length are still on the intuitive level, (Zubin, 1965).

It is interesting to note that psychology as well as psychopathology cede their hard-won gains to other fields, once the subjective experience has been transmuted to objective data. Thus, in psychology, a large part of psychophysics has become the domain of illuminating and acoustical engineers; educational psychology has been taken over by the educators; while in psychopathology, general paresis, as soon as its etiology became known, was lost to the field, as were pellagra with psychosis, epilepsy, phenylketonuria, etc. Psychopathology retains only the diseases of unknown etiology, and psychology deals only with the still generally intractable aspects of experience. The applied fields take over everything susceptible of measurement.

Turning now to the present symposium, its theme is "Biological and Psychological Correlates of Psychopathology" and in carrying out this theme, after a historical introduction by the Mahers the presentations move on to genetics, biochemistry, psychology immunology
and gerontology and geriatrics with special reference to Alzheimer's Disease.

These 5 areas are indeed at the cutting edge of psychopathology today but I wish the symposium could have lasted longer to include contributions from the social-cultural or ecological fields in which such important concepts as social networks and life events are impacting on psychopathology and from the learning theory field which has blossomed into the utilization of cognitive forces in the etiology and treatment of psychopathology.

In trying to anticipate the specific contribution of the contributors, I decided that the best a summarizing discussant can do is to prepare a procrustean framework for integrating the contributions, so that come what may, he will have something to say on the contributions of each speaker to the proposed integrative theme. I hope I will not cause any of the truncations or elongations that Procrustes himself indulged in, in laying his guests on his prearranged bed!

The integrating thread that I am going to propose is the vulnerability hypothesis, and though it has been formulated primarily with regard to schizophrenia, I think that it can also serve as a framework for the other mental disorders in the field of psychopathology. As a matter of fact, Brendan Maher, Raymond Crowe and Bonnie Spring, have already referred to the hypothesis in their papers.

The vulnerability hypothesis which was first promulgated in 1961 at a symposium on "Recent Advances in the Study of Behavior Change" held at McGill University in 1962 (Zubin, 1963), postulates first that episodes of illness will occur in an individual who has either inherited or developed a degree of vulnerability to an illness which will be elicited when a sufficiently stressful life event stressor impacts on the individual. However, certain moderating variables may either absorb the stress and thus abort the episode or enhance the stress and thus make it more probable.

Thus even vulnerable individuals who meet with a sufficiently stressful life event need not develop an episode if such benign factors as a good social network, a good ecological niche or a good premorbid personality are present.

In order to test the hypothesis, it becomes necessary to develop means of identifying the vulnerable. To this end, a search for markers of vulnerability has begun in various laboratories including those under the guidance of Professors Sutton, Kietzman, Spring, Holtzman, Buchsbaum and our own laboratories as well as in many other laboratories. For a marker to be a vulnerability marker it must
satisfy the following conditions: (1) Be present premorbidly, morbidly and post-morbidly in the proband (2) be present in unaffected first degree relatives of the proband.

We must also have markers of beginning and end of episodes in order to be able to establish the episodic nature of the disorder. We must also have measures of the moderating variables (social network, ecological niche and premorbid personality) in order to be able to explain why some vulnerable people exposed to stressful stressor do not develop episodes.

The vulnerability hypothesis is in some sense a heretical hypothesis flaunting the accepted dogmas of the psychopathological establishment. These heresies are:

1. Schizophrenia is far more benign in outcome than what we have been led to believe.

2. It is an episodic disorder and not the persistent chronic condition that DSM III makes it out to be - the only persistent quality it has is vulnerability on the part of the patient to the development of one or more episodes.

3. Chronicity is not an essential part of its natural history but reflects either the persistence of premorbid personality or iatrogenic, ecogenic, or nosocomial artifacts. This also holds true of the negative symptoms which go along with chronicity.

4. It is a unitary rather than a multiple disorder, but may arise in a variety of ways.

It must be remembered that the heresies of today often become the dogmas of tomorrow which in turn give way to the heresies of the day after tomorrow. Luckily, there are no more burnings at the stake!

We can encapsulate the essence of the vulnerability approach in the following statement: While the established view regards a person who has, or has had, a schizophrenic episode as an essentially sick person who sometimes has intervals of wellness, the vulnerability view regards such a person as an essentially well person who has intermittent episodes.

Before proceeding with the summary of the papers let me point out the various schools of etiology now clamoring for admission into the pantheon of psychopathology.

Elsewhere (Zubin, et al., 1985) I have indicated that the following etiological models have been proposed for schizophrenia: (1)
ecological, (2) developmental, (3) learning theory, (4) genetic, (5) internal environment, (6) neurophysiological and (7) anatomical. Each of these has its own school of devoted adherents and it is in these models that we search for the presence of markers.

Beginning with the Mahers' scholarly historical perspective on the study of psychopathology it becomes clear that our attitude toward psychopathology across the ages reflected the prevailing zeitgeist. Currently there seem to be two trends contending for the soul of psychopathology. First, the economic squeeze on the mental health expenditures with the demand for containing the inflation of medical costs has given rise to a Neo-Kraepelinian revolution demanding rigid criteria for diagnosis and prescriptive limitations on duration of therapy in order to standardize payment by means of the DRG (Diagnosis Related Groups) with specified limits on payments for each diagnostic grouping. On the other hand, the civil rights and human rights movements have begun to doubt whether commitment procedures and hospitalization of the mentally ill are not invading private lives illegally. The recent data from European long term follow up studies with their optimistic benign outcomes stand out in stark contrast to the rather dismal outcome statistics in our own country. The vulnerability hypothesis, provides a balance between the Neo-Kraepelinian dire approach to outcome in schizophrenia and the more optimistic winds blowing in from Europe by pointing out that much of the chronicity observed in the USA may be an artifact produced by iatrogenic ecogenic and nosocomial (hospital produced) forces, (Zubin, et. al.,1985).

But it is interesting to inquire how the attitudes adopting the malignant deteriorating aspects of schizophrenia developed in the first place. The Zeitgeist that permeated Western culture during the latter part of the 19th century when Kraepelin developed his nosology indicates that a "Degeneration Hypothesis" was in the air, (Zubin, 1985). Both Benedict Morel (1809-1873) and Valentine Magnon (1835-1916) argued that mental disease reflected the presence of a degenerative hereditary strain which becomes progressively more severe in successive generations. The ultimate consequence of this process would be the extinction of the line. The fatalism engendered by the possession of this taint produced the belief that even the unaffected family members carry the seed of destruction within them.

Bonnie Spring's quote in this symposium from Torrey regarding the mother's wish that her daughter would be better off having leukemia rather than schizophrenia and Kurt Schneider's alleged advice to the families of schizophrenics that their relative is hopeless and the best they can do is to go home and forget him/her are further examples.
The "Degeneration Theory" seemed to permeate the Zeitgeist at the turn of the century and probably also expressed itself in the eugenics movement in England in which Galton and later, Pearson, tried to prevent the degeneration of the English gentry through limiting immigration and selective breeding. It is likely that in the USA the study of the Kalikaks and Jukes was launched by the same Zeitgeist. Whether this Zeitgeist influenced Kraepelin and made him apply the degeneration hypothesis to dementia praecox is a moot point requiring historical investigation, but it seems a plausible hypothesis.

It is somewhat unfortunate that the economic pressures of our day serve to revive this degeneration and deterioration hypothesis in DSM III. It is probably one of the reasons why families are ashamed of schizophrenic relatives - the fear of degeneration is still in our Zeitgeist despite the evidence from modern genetics and how to counteract it is one of our basic social problems. It is one of the reasons why I find the vulnerability hypothesis, even if it still has to prove itself, more gemutlich than the NeoKraepelinian approach.

The Mahers' scholarly analysis of the early history of mental illness devolves into a historical analysis of the models of mental disorder which were most prevalent at each period.

Although it is true as the Mahers point out that historical reviews of the field of mental disorders are fraught with danger of error, it is rather interesting to note that scholarly historians have managed to discover historical documents such as hospital bills which through proper statistical manipulation utilizing the actuarial methods of capture-recapture of mobile animals population counts in the wild, yield information even on the prevalence of at least treated mental disorders in the 16th - 17th century in England (Neugebauer, 1984).

There is also considerable evidence that witchcraft was not the only alleged cause of mental disorder (Neugebauer, 1984). Similarly, Dain has succeeded in the unravelling much of the history of mental disorders in America during the colonial period.

The Mahers suggest that the mind-body problem which is perhaps still the most fundamental question regarding the nature of mental disorders (is the fault in brain or in mind?) was a question which only philosophers were concerned with. Those who dealt with mental disorders regarded them as physically based and treated them with physical means. The physical models covered are (1) bioelectrical, (2) physical debility, (3) general vulnerability model involving stress, (4) infectious disorder, (5) humors disturbances (blood, digestion), (6) brain pathology and (7) genetic models.
In addition they discuss several non-physical model such as will power and character.

The Mahers' presents one of the most fascinating descriptions of the nature of the bioelectrical disturbance conceived as a model for mental disorder, relating it to the electric nature of the neural impulses, amount of energy available within the organism and its maldistribution as a possible cause of hysteria and asthenia. It might be of interest to refer to the fact that in Cicero's day electric eels were used to shock mentally ill patients – perhaps the first use of ECT.

It is also interesting to note that the attribution of mental disorder to deficiency in energy constituted some of the early guesses made by Freud on the lowered energy of cells and formed the basis for Van Gieson's hypothesis regarding the role of energy levels in the cells of the mentally ill.

That the bioelectrical model was one of the first to hold sway in psychopathology soon after Galvani's discovery should not be surprising since science is always at the mercy of new inventions. In fact, scientific advances occur much more often as the result of such technologicla advances as microscopes, telescopes, cat scans, etc., than they occur as a result of theoretical developments (Zubin Models for Etiology of Schizophrenia).

Debility as a source of vulnerability to breakdown is elegantly described in Burton's Anatomy of Melancholy and we owe the Mahers a great debt in tracing back the currently popular life event schedules to Burton's work.

One of the most striking examples of physical debility as a basis for the development of mental disorders was promulgated in the early 1920's by Henry Cotton in New Jersey under the name of Fecal Infection Theory. It took the efforts of Kopeloff and Cheney at the New York State Psychiatric Institute to demolish this theory by conducting the first clinical trial in psychopathology in the USA. He removed all the foci of infection from a group of patients (caries teeth, infected adenoids, tonsils, colons, turning many a colon into a semi-colon) but found a difference only in the morality rate of the operated cares compared to the controls.

One wonders whether Gerald Macauras' treatment of thirty patients connected in series to a source of electrical current preceeded the development of psychological group therapy procedures.

The Mahers summary of the view of the etiology of mental disorders is that is "arises through changes in bodily states that may be brought about by either biological agencies and/or a range of
environmental stressors." They indicate that purely mental etiology was only a brief intermittent interruption in the course of history. This view is very attractive and provides for the interaction between biological and environmental factors, a view which is most agreeable to many. However, this view could be interpreted as signifying that man is a pawn in the hands of his biological inheritance and environmental engulfment. As was already stated, such an interpretation of the view of the Maher's renders man and automaton without playing any role himself. I do not believe that this interpretation is tenable.

One of the most exciting papers was that of Christopher Coe on Psychoimmunology, perhaps because it is a brand new idea to me. Before coming to this symposium the question of how the external stressful events enter the central nervous system to bring about the experience of stress has always bothered me. Once I began following Coe's ideas and especially the promulgation of these ideas in Robert Ader's edited book on psychoneuroimmunology, I began to realize that the central nervous system, the neurohumoral system and the immunological system interact with one another in a variety of ways. The perception of the external event via the central nervous system is sufficient to set the interaction in motion. How this interaction proceeds is the question of the day. It is not unlike the question of how information processing takes place. Perhaps the where, when and how questions we have posed and successfully answered to some extent in information processing can serve as a paradigm for "stress" processing. Dr. Coe's work fits nicely into the developmental model (Zubin, 1972) and also indicates how the life stressors which serve as triggers in our vulnerability model operate. It also fits into our concept of chronic stress which can serve as a formative factor in vulnerability theory (Day, 1985) and provides the mechanisms by which stress become an integral part of the internal environment.

That personality traits and emotion can affect susceptibility to disease gave rise to the school of psychosomatic medicine including the complementary somatopsychic conditions. But as Coe points out, these schools dealt only with the endocrine system, autonomic system and their interrelationships with the central nervous system but not with the immune system. The importance of the latter burst upon the clinical horizon rather precipitously perhaps in the wake of Selye's work on thymolymphatic involution as part of the General Adaptation Syndrome in his theory of stress. It is likely that the moribund psychosomatic movement got a new lease of life from the rise of immunology.

Coe reviews the literature on the immunological consequences of psychological disturbance in a masterful way, giving first the basic underpinnings of immunology developed during the last few decades. This is followed by a bird's eye view of epidemiological research
dealing with the role of life event stressors in initiating stress in relation to physical disorders which implicated a reduction in the effectiveness of the immune system as a bulwark against illness. In doing so, the role of such moderating variables protecting the immune system from breakdown as the social network, premorbid personality and the general life style of the ecological niche occupied by the person, are pointed out. The impact on the immune system of such stressors as unemployment and bereavement and loneliness are documented. More recent attempts have been made to trace more specifically the connection between specific stressors and specific changes in the immune system, a sort of tracing of the process from the stressor to its effect on the immune system. An exciting finding is reported regarding the impact of verbal articulateness and ability to express emotion on lowering the rate of mitosis and an increase in lymphocyte counts at the tumor site in persons with good outcome, in contrast with those of poor outcome who were inarticulate and unable to express emotion. Here we have in a sense a measure of the state of the immune system under degrees of stress. Thus, the status of the immune system can demonstrate the degree of stress a mental patient is experiencing even when he can not articulate it or report it. But even more important is the possibility that the monitoring of the immune system in recovered patients may yield information regarding impending relapse. At present, all we have to go on is the report of the outpatient who returns for a check up, a most unreliable source of the presence of absence of stress compared to cellular measures provided by the functioning of the immune system. The controversial problem of whether stressor-triggers are required to elicit an episode in a vulnerable person, which formerly could be inferred only from life-event interviews can now be buttressed by immunological measurements. This perhaps is the most important contribution Coe makes to this symposium.

The breakdown of the immune system under stress presents us with a paradox. If the function of the immune system is to serve as a bulwark against stress, the reduction of immune activity when it is most needed under stress is a maladaptive response and should have been selected out by evolutionary forces so that only those whose immune system resisted reduction would survive. What survival function the reduction in immune activity may serve is indeed a moot question.

Professor Spring points out that the scientific model we adopt for schizophrenia will color our attitudes towards it and constrain our expectancies for its outcome. I am reminded of Rene Dubos' comments regarding the imperialism of biological causality. According to Rene Dubos, the biological approach assumes that "all the constituents and processes found in living things including man, obey the laws of inanimate matter." In describing the proceedings of a recent international congress on "From Theoretical Physics to Life,"
Dubos indicates that though general agreement was reached on the above statement, the moment the discussion shifted to the bearing of scientific knowledge on human behavior and on social action, pandemonium reigned.

"We know a great deal concerning the physiochemical phenomena that make life possible, and we can formulate reasonable hypotheses concerning their origin and evolution. We can imagine, even though we do not completely understand, how each particular living thing is shaped by genetic constitution, experiences and environment...the physiochemical forces provide (however) only the props and stage machinery," (Dubos, 1971).

By the same token, the environmentalist may be guilty of not recognizing the role of biology as a major factor in treatment. Thus, permitting a patient to writhe in his episode when at least temporary if not permanent relief is available in drug therapy, is an unforgivable error!

Thus far we have described the etiologic models as blind forces which control man's destiny and to some extent, given the current scene, this is a true picture. For the ecological niche in which man finds himself does determine his well-being, his genetic make-up does limit his potential, his developmental past and learned behavior do confine his future, his internal environment and neurophysiologic make-up control his behavior. In fact, we might agree with Dubos, that all of these forces are merely the stage props for the drama that man is to enact on the stage of life. However, we have omitted perhaps the most important determinant of man's stage behavior—his ability to be a self-starter, to alter developmental trends, to modify the internal environment as well as his neurophysiologic equipment. Unlike other organisms which are shaped by their environment through eons of gradual evolutionary developments, man can shape his own environment if he chooses to do so and has developed the know-how to apply changes not only to the exogenous but also to the endogenous environment. It is in these directions that the future of man's normal development, as well as the containment and improvement of abnormal development, lies. It need not take eons to accomplish, for we can produce changes for the better even in our own lives and within our own lifetime. The options that such changes make possible are the real problem we are facing. How are we to decide what changes to bring about, and where does the moral and ethical imperative come into play? I am afraid that such questions are beyond my ken, and perhaps beyond the ken of science. Nevertheless, they are issues which we cannot help but face, and only by increasing our scope to include within our ranks philosophers of science and ethical and moral scholars, can we hope to come to any agreement on these issues (Zubin, 1972).
Dr. Spring points out correctly that neuroleptics deal primarily with the state of the individual - the episode - but do not impinge as far as we can tell now on the inherent vulnerability of the person. This vulnerability antedates the episode and persists after it, as indicated by the occurrence of relapses. It is debatable, however, whether this vulnerability affects the person when not in an episode, and may remain latent, in at least some patients in the interim between episodes, even as it may remain latent for life in those vulnerable individuals who never develop episodes. For this reason, the negative symptoms reflecting vulnerability (p. 10) may apply only to a still undetermined proportion of patients. Nor do we need to conclude that patients who persist in negative symptoms present a different disorder from the others. The heterogeneity of schizophrenic behavior may be due not so much to different disease processes as to (1) different premorbid personalities (2) different ecological niches and (3) different pathways utilized in attaining the episode even though the final end-state of the episode may be a common feature of all schizophrenics.

One point raised by Dr. Spring is the question of whether cognitive vulnerability markers detect a predisposition or an actual risk of schizophrenia (p.15). I interpret this distinction to mean that predisposition refers to a possibility of developing an episode which may in fact never occur, and an actual risk refers to a prediction of occurrence which is much higher than in the general population or in members of families with a negative history for schizophrenia. This is a rather refined discrimination which at the present time cannot be of empirical value, though it is of great theoretical value. To make the case even more complicated, Manfred Bleuler has suggested that though genetics play an important part in the predisposition for schizophrenia it is due not to the transmission of any particular set of alleles but rather to the fact that the individual has inherited a set of conflicting genes e.g., genes which represent sensation seeking behavior, and genes which represent withdrawing tendencies. The incompatibility of these two trends may present a conflict, not unlike Freud's suggestion of unresolved instinctual conflicts as a source of schizophrenia. Thus, according to Bleuler we may never find the particular combination of alleles for schizophrenia because they do not exist. This may also explain why so many patients hail from non-affected families. The transmission may be genetic, but not systematic and the probability of concurrences of the same genetic anlage in two members of a family may be very low and even the concurrence of two different but vulnerable anlagens may be even lower. Incidental evidence encouraging this view comes from the suggestion of Matthysse that the genetic anlage for deviation in smooth pursuit eye movements, and the genetic anlage for schizophrenia are independent expressions of an underlying latent trait. Thus, good eye tracking schizophrenics may have first degree relatives that are either good or poor trackers while similarly bad eye-tracking
schizophrenics may have good or poor trackers in their first degree relatives. Nevertheless, poor eye tracking and schizophrenia may be both expressive of an underlying latent trait. If this is true, it could follow that other pair of genetically based traits may be expressive of the underlying vulnerability and the possibility that they may be antithetical can, at least theoretically, be entertained.

The issue that Dr. Spring raises regarding whether vulnerability markers reflect maladaptive cognitive strategies or physiological dysfunction is a rather intriguing question. First of all, we must separate linkage markers from pathophysiological markers. A linkage marker is an innocent bystander that has nothing to do with etiology but happens to be linked to basic etiological genes by geographical proximity on a chromosome, like color-blindness in relation to effective disorder. The question then is, do pathophysiological markers reflect maladaptive cognitive strategies or physiological dysfunction. I would, for reasons of parsimony and elegance, the only criteria available in the construction of theoretical models when no empirical guidelines are available, prefer to place maladaptive cognitive strategies into the premorbid personality, one of our moderating variables, rather than making it part of the vulnerability factor. Further reasons for this is the fact that not all individuals with maladaptive cognitive strategies develop schizophrenic episodes. According to my proposal they must first have the vulnerability for schizophrenia and then when they are subjected to stressors will be unable to contain them for lack of suitable cognitive strategies. Furthermore, it is likely, following Jerry Kagan, that adaptive cognitive strategies develop naturally in the course of living in most intact people, even in the premorbid period of those who later develop episodes of illness, but some individuals lose these strategies for lack of reinforcement. Perhaps their reinstatement is necessary before they can successfully cope with the stressors that tend to elicit vulnerability. Until we get more observations on how vulnerability works, the question remains moot.

Regarding the utilization of slow reaction time, crossover reaction time and crossmodality reaction time, the last word has not yet been said on the contribution of each. The fact that as Kaplan has shown that training can adjust the slow reaction time to normal levels, would argue that it may be more a reflection of the general deficit syndrome than of a basic deviation. Recently, Manuzza ( ) has shown that the crossmodality technique has certain advantages because it yields individual scores that differentiate schizophrenics with little if any overlap from controls. The crossover technique rests primarily on a group difference. However, the cross over technique has been found to characterize unaffected siblings while the crossmodality technique has not yet been shown to do so. Further work is necessary before this problem is resolved.
It is interesting to note that as far as the explanations for the cross-over and cross-modality phenomenon go, (Oldiges, 1985) who has compared the segmental set theory of Shakow with the neural trace theory of Zubin concludes that he found no evidence for the segmental set explanation but considered the neural trace theory as promising.

Two very exciting findings are Dr. Spring's finding that dichotic listening with distraction may serve as a vulnerability marker and the finding that the primacy effect but not the recency effect in memory tasks under distractions may similarly serve as a vulnerability marker. In an attempt to explain the findings, Dr. Spring makes the ingenious suggestion that capacity for information processing may be at fault in one of three ways.

First, there may be a reduction in capacity to deal with the distracting tasks because of brain dysfunction. Second, it may be due to distribution of attention requiring more effort because even the unattended channel in dichotic listening is attended to by schizophrenics. The loss in "primacy" in memory may be due to poor strategy in the case of the memory task such as may occur when automatic processes are not utilized and effortful procedures are required. There is still a fourth possibility, and that is, that the capacity is intact but that coping ability is at fault, perhaps reflecting the general deficit syndrome when task-demand increases. How can one distinguish between these four possibilities?

Dr. Spring makes the very plausible suggestion that the effect of practice in the several tasks may reveal the cause of the disability. Laying aside the possibility of brain dysfunction, practice sessions with instructions should eliminate the misuse of strategies, and probably also the faulty application of processing capacity. It is difficult to see how it could uplift coping ability, unless the exercise proves to be therapeutic.

As regards the brain dysfunction possibility, it is difficult to predict whether practice may not produce an improvement by engaging substitute brain processes which are not damaged. However, it is likely that this would require a great deal more practice than the other methods. But it should be borne in mind that the elimination of these deviations by practice should not eliminate them as markers in unpracticed individuals.

As to distinguishing between these possible explanations more directly, perhaps suitable monitory of the information processing task may yield the answer.

Dr. Crow presents a scintillating review of research in psychiatric genetics and illustrates it with an application to panic
It is interesting to note that because research in the functional disorders (schizophrenia and affective disorders) is now treading water, interest has shifted to the milder conditions, especially the neurosis of panic disorders. It is to be hoped that the 'escape' into panic will not be permanent and that interest in the functional disorders will resume when the current flurry in panic passes.

Since the only basis available for studying genetic disorders is through the studies of relatives consanguinous with probands who are now having, or have had, an episode of the disorder, it becomes clear that we must resort to population genetics as our primary point of entry. This leads to utilizing epidemiological technics ranging over the entire spectrum from group to individual behavior and characteristics and down to the molecular atomic levels. He raises the primary questions that are to be answered by genetic investigation: (1) demography of the disease, (2) is it transmitted within families, (3) does the transmission involve a genetic anlage, (4) what is the genetic mechanism and (5) how do the genes produce the disorder.

He points out that epidemiological studies will answer the first question; family studies, the second; twin and adoption studies, the third; the next step is to weave the data yielded in answering the above questions into a framework that will permit postulating genetic models to explain them and for this purpose genetic markers an appealed to.

Applying these procedures to panic disorders he emerges with the following noteworthy generalizations. (1) panic disorders run in families, the risk in families of probands being about 8-fold when compared to the general population; (2) women have a much higher risk (2 to 3 times as high as men); (3) age of onset is in the late 20's; (4) this familial transmission is specific to panic disorders only; (5) twin studies give definite evidence for genetic transmission, but since no adoption studies have been carried out, the role of environmental factors in the transmission can not be ruled out. However, since the concordance rate falls far short of 100%, the penetrance is far from perfect and environmental factors must play a role at least in the elicitation of vulnerability if not in the actual transmission of even the genotype that does not reach phenotypic expression. Assuming that there is a genetic component to the transmission of panic disorders, the question arises whether it is monogenic or multifactorial-polygenic. The available data are not capable of distinguishing between these two possibilities in the absence of a biological marker for the disorder which is more closely tied to the genome than is the clinical diagnosis.
There is a possibility that infusion of sodium lactate may serve as a biological challenge to elicit the vulnerability to panic disorders even as amphetamine can serve as a challenge to elicit an episode or its exacerbation in schizophrenia. Furthermore, these induced attacks can be blocked by imipramine, which also blocks spontaneous attacks, suggesting that there is a great likelihood that the induced, are no different from the spontaneous, attacks.

The gender difference in the prevalence of panic disorders when considered against such other gender differences as the delayed emergence of schizophrenia in females and the better outcome in females, might suggest that the stronger family ties in females may play a part. In the case of schizophrenia, the vulnerable females are protected by the more intimate family relationships and the returned recovered female may be subject to less risk of relapse. But there is a price to be paid for the increased protective intimacy in so far as it may foster overprotectiveness. The female, vulnerable to panic attacks, may be ill-prepared to meet the daily hassles of life on her own and may thus be more prone to develop an episode. Thus, as Crowe suggest, the gender difference may not be in vulnerability, but in phenotypic expression.

Dr. Crowe's discussion of the genetics of anxiety raises an interesting contrast between psychosis and neurosis. According to our vulnerability hypothesis psychosis is a state or is episodic in nature while neuroses are traits or permanent characteristics which may vary in intensity depending upon environmental contingencies. Thus, since vulnerability itself is a trait, neuroticism is another personality trait and cannot easily be dissected out of vulnerability. It may, therefore, be more difficult to find vulnerability markers for neuroses although we may be able to find predictors early in life of the eventual development of a neurosis. It is also interesting that there have been studies indicating the genetic basis for neurosis going back to the 40's. Somehow these studies did not catch on until now. (Discuss anxiety and psychosis from McGill paper.)

Dr. Hutton reviews the etiologic theories of Alzheimer's Disease ranging from (1) unconventional viruses; (2) genetics to (3) autoimmune approaches.

Hutton reviews the evidence for the unconventional virus indicating the similarity between Alzheimer's disease and those diseases of known viral etiology but indicates that since transmission of the disease by inoculation which was successful in the viral diseases could not be demonstrated in Alzheimer's disease, the evidence for viral etiology can not yet be accepted. As far as the genetic etiology is concerned, though the risk is higher in relatives than in the general population, it is not sufficiently higher to provide overwhelming evidence for a decisive genetic component. As
regards the autoimmune system as a source of etiology, the decreased ability of the immune system to differentiate the body's own cells from foreign cells, tends to produce attacks on one's own tissues and on this basis an autoimmune hypothesis can be entertained. Although there is no overwhelming evidence for any of these hypotheses, he concludes that though no definitive evidence for the tenability of the first two etiological theories can be documented, there may be some tentative evidence for the third. This conclusion is based on the fact that a significant increase is found in the frequency of serious head injuries in Alzheimer victims compared to hospital controls. It is postulated that these head injuries may damage the permeability of the blood-brain-barrier with resulting immunological sensitization to brain antigens. This immunologic sensitization may be accompanied by the entrance of neurotoxic serum proteins, unknown toxins, or an unconventional virus. Genetics may play a role in raising the risk for each of the above events.

It is also possible that the frequency of head injuries may reflect either a prodromal factor or an inborn tendency for accident proneness. Thus, even in such an apparently biologically based disorder as Alzheimer's disease, the role of vulnerability in inducing an interaction between the biological and environmental factors may be a necessary condition for the development of the disorder.

One wonders whether the recent claims of the nucleus basalis as the seat of Alzheimer's disease has furthered knowledge enough to provide an integration of the scattered findings. Furthermore, if the immune system is an important factor, can the demonstrated effects of social networks and other psychosocial variables on the integrity of the immune system play a part in the approaches to the treatments of this disorder.

**SUMMARY**

The overall conclusion that emerges from this symposium is that neither biology above nor ecology above can be themselves explain the etiology of psychopathology. This is perhaps such a foregone conclusion that a symposium focused on proving this now obvious axiom would be redundant.

Nevertheless, as one reads the literature, it becomes clear that advocates of each of the four biological models (genetic, internal environments, neurophysiological and neuroanatomical) have their zealous believers and that each of the three environmental models (ecological, developmental and learning) are not lacking for zealous devotees.
For this reason, a careful review of each of these points of view should serve to integrate the need for a common framework such as is provided by the vulnerability hypothesis. It also becomes necessary to make a place for the immunological model in the pantheon of scientific models in order to give it its proper recognition. I do this with some hesitation since it is perhaps possible that the immunological system may not prove to be etiological but more of a triggering factor.

However, if the immune system is found to be involved in the development of psychopathology over and above its use as an indication of stress, it should be a rightful member of the pantheon.

The reader may be somewhat puzzled by the disparity in the treatment of the various chapters. This puzzled me too, at first. But on further thought it became apparent to me that the disparity reflected not the relative importance of the contributions but the limitations of the reviewer. I was far more acquainted with some of the topics and in these chapters I was able to be appreciative as well as benignly critical. In the others, I could be only appreciative, since my knowledge was enhanced by those chapters, but I had no sufficient background for critical evaluation.
REFERENCES


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