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During the past two decades, increasing numbers of research projects have focused attention on those children who have a high probability of developing a major psychiatric disorder in adult life. These studies are subsumed under the rubric "risk research" and have been directed for the most part toward determining which children are most vulnerable to eventual schizophrenic illness. Affective disorders have only recently begun to be studied in similar fashion.

"Risk" refers to the greater likelihood that certain individuals will develop a mental disorder than will others selected at random from the same community. The children of schizophrenics, for example, are at greater than average risk for developing schizophrenia than the general population (10 to 15 percent for the child with one schizophrenic parent compared with approximately 1 percent for a child with nonschizophrenic parents).

"Vulnerability" implies that each individual is endowed with a degree of vulnerability to illness that under certain circumstances will become manifest. In one vulnerability model two major components are described—inborn and acquired. Inborn vulnerability refers to that which is in the genes and is reflected in the internal environment and neurophysiology of the organism.

The acquired component is due to the influence of specific diseases, traumas, perinatal complications, family interactions, and life events that either enhance or inhibit the development of future disorder. For an individual vulnerable to schizophrenia, for instance, periods of acute stress may result in a failure of coping mechanisms so that maladaptation results. According to Arieti, Adolph Meyer became convinced that dementia praecox resulted from inefficient coping mechanisms which led to eventual breakdown. Meyer believed there was either a gradual transition to a schizophrenic episode or an acute onset precipitated by a catastrophic event. In contrast to vulnerability, "invulnerability describes the organism's ultimate resilience to the load imposed on it by life event stressors" [p. 114].

Goals of High-Risk Research

Erlenmeyer-Kimling has summarized the goals of high-risk research as follows: (1) development of the natural history of the disorder being studied; (2) identification of the specific members of the high-risk group most likely to become affected; (3) determination of early predictors of the disorder, particularly those indicative of underlying biological deficits; and (4) examination of the various factors, environmental in nature, that increase the likelihood of prepsychotic illness becoming manifest as well as those that may protect a vulnerable individual from becoming ill.

An additional far-reaching goal of high-risk investigations concerns the question of intervention. If one could detect the vulnerable child and provide competence-enhancing interventions, could the future patient be sufficiently protected so that subsequent illness could be prevented? Current research is undertaking the examination of biological, psychological, and sociological factors that may be conducive to the development of schizophrenia and affective disorders.

Children At Risk for Schizophrenia

"Schizophrenia," which Bleuler coined in 1911. is a concept that is still developing and changing today. Bleuler renamed Kraepelin's term, dementia praecox, because he considered "splitting" of the different psychic functions one of the most important characteristics of the condition. Schizophrenics are well known to constitute a heterogeneous group (paranoid, hebephrenic, catatonic, and simple). There are marked differences in terms of genetics, biochemistry, symptom clusters, course, and outcome. Langfeldt tended to lump the schizophrenias into two principal groups, process and reactive (which other investigators have called chronic and acute). Other labels have indicated that an individual may demonstrate some schizophrenic attributes without ever having been psychotic (that is, the nonpsychotic schizophrenic or schizotypal personality). The concept of a schizophrenic spectrum embraces these categories. Such diverse diagnostic considerations have made

past research efforts unwieldy, and collaborative efforts difficult. Thus, research diagnostic criteria have evolved that define more sharply the illness under study. Strauss and associates have defined schizophrenia, for example, as “a psychiatric disorder without demonstrable organic etiology that is manifested by such phenomena as delusions, hallucinations, bizarre behavior and thought disorder in which manic or depressive features are not predominant.” Numerous models for the transmission of schizophrenia have been promulgated. At the core of research into high-risk schizophrenia is the question of whether a given deficit in premorbid adjustment is sufficient to cause a schizophrenic breakdown in later life, or whether a particular environmental stress is necessary for the development of the illness.

Etiological Models for the Transmission of Schizophrenia

Psychogenic Models

Various etiological models have been reviewed in the current psychiatric literature. Proponents of the psychogenic theory of the transmission of schizophrenia contend that abnormal patterns of family interaction are largely responsible for pathological adaptation and subsequent schizophrenic breakdown. Wynne and Singer have viewed the future schizophrenic as an individual highly vulnerable to a disorder in family communication. Bateson and associates have, in fact, labeled that individual

chiefly responsible for extreme confusion in the young child as the "double bind" mother. They contend that the double message provided by an extremely ambivalent parent and the subsequent failure in family communication is instrumental in setting the stage for subsequent breakdown in thought and communication in the vulnerable child. Because distortions of reality are so frequent and denial on the part of the ill parent such a prevalent defense, the child subjected to intense and frequent "double bind" communication is unable to acknowledge his own perceptions as being accurate.

Lidz and his collaborators have also been proponents of a psychogenic theory that holds that severe chronic disequilibrium and discord (marital schism) and submission to pathological attributes of the schizophrenic parent (marital skew) are primary etiological factors in later schizophrenic breakdown.

Genetic Models

Genetic approaches to the study of schizophrenia have been in existence for six decades. Franz Kallmann was the chief proponent of the theory that the more closely related an individual was to a schizophrenic relative, the greater was the likelihood of his becoming schizophrenic. Kallmann, studying monozygotic and dizygotic twins pairs, held that if one monozygotic twin was

known to be schizophrenic, the risk to the co-twin also schizophrenic was 86 percent. Recent studies, using sophisticated techniques and "blind raters," achieve a concordance rate of 42 percent for monozygotic twins as against 10 percent for dizygotic twins, approximately the same as sibling rates concordant for schizophrenia.

Since the twins were usually reared together, opponents of the genetic theory argued that environmental influences should not be underestimated. The adoption studies have removed that variable by examining offspring of schizophrenic mothers reared by foster mothers. Heston demonstrated that of forty-seven adult offspring of schizophrenic mothers who were adopted within the first few days of life, 10 percent developed schizophrenia in adult life opposed to none in the control group (children of nonschizophrenic mothers adopted at birth by nonschizophrenic women). When Kety and Rosenthal, using a Danish population, corroborated Heston's findings, they found that the incidence of schizophrenia among the biological relatives of adopted schizophrenics was six times as high as the incidence noted among the relatives of the control adoptees. Wender and associates moreover, reported a cross-fostering study in which adopted offspring of normal biological parents were reared by schizophrenic adoptive parents. These children were compared with: (1) adoptees of normal biological parents reared by normal adoptive parents; and (2) adoptees of schizophrenic biological parents who were then reared by normal adoptive parents.

Wender and his collaborators noted a significantly higher prevalence of psychopathology among the adopted offspring of schizophrenic parents in contrast to the other two groups.

Summary of the Evidence in Support of Hereditary Factors

1. Schizophrenia-like behavior has been reported from antiquity to the present day and occurs in both industrialized and undeveloped societies.

2. The prevalence throughout the world is 8 to 1.5 percent, although there exist isolated populations with higher and lower rates.

3. The male-female ratio is one to one.

4. In urban communities there is a marked social-class gradient in the prevalence of schizophrenia, usually attributed to a premorbid "downward drift" of predisposed individuals.

5. No environmental causes have been identified.

6. Frequently there is no known precipitating event.

7. Risk figures are compatible with a genetic hypothesis.

    a. First degree relatives of schizophrenics are at greater risk of becoming schizophrenic compared to the general population (5.5 percent for parents, 10 percent for siblings, 11 percent for children).

b. Monozygotic-twin concordance rates for twins reared apart are approximately the same as for twins reared together. They are three times as high as the concordance rates for fraternal twins.

c. Concordance rates in monozygotic co-twins vary with the degree of severity of illness in proband; high concordance rates are associated with severe illness.

d. Schizophrenia occurs at the same rate in children of affected fathers as in children of affected mothers.

e. The risk for children of two schizophrenic parents is three times that for children of one schizophrenic parent, whether the children are reared by their own parents or not.

8. Adoption studies have demonstrated:

a. Children of normal parents who are reared by schizophrenic adoptive parents do not have an increased rate of schizophrenia.

b. Children of schizophrenics adopted by normal families develop schizophrenia at the same rates as those of children reared by their own ill parents.

c. Unlike the biologic relatives of schizophrenic adoptees, the adoptive relatives do not have elevated rates of schizophrenia.

9. There is no significant increase in schizophrenia risk among

children with early deafness, despite the communication difficulties they experience.

10. Family members of individuals who develop schizophreniform psychoses following head injuries have risk figures equal to the general population, unlike the figures for families of "true" schizophrenic probands.[1]

Regarding the strength of the genetic factor in schizophrenia and the mode of transmission, the best available evidence points to the likelihood that a genetic factor constitutes a necessary, though not sufficient, antecedent. Although the predominant mode of transmission may be polygenic, Matthysse and Kidd have shown that a single-major-locus model cannot be discarded. Heterogeneity may also be present in the sense that individuals classed as schizophrenic may be regroupable as belonging to several differing patterns of transmission or to different sets of noxious genes.

Evidence in Support of Environmental Influences (Diathesis-Stressor Framework)

Despite the fact that monozygotic twins share all their genes in common, more than half of the pairs are discordant for schizophrenia. In other words, factors other than heredity are responsible for either protecting a constitutionally vulnerable individual from breakdown or for precipitating a breakdown. According to the diathesis-stressor framework, genetic predisposition, or diathesis, comes under the influence of environmental

stressors which eventually result in physiologic and biochemical change in the organism.

Gottesman has stated that to date no environmental causes have been found that will invariably produce genuine schizophrenia in persons unrelated to a schizophrenic. However, the contributions from environmental stressors determine for each individual the point at which a clinical threshold is passed. Gottesman stated: "Starting with a subject's genetic liability for schizophrenia at birth, one then adds psychological stress over time that has the effect of adding to his liability" [p. 36]. Stress factors may include chaotic home life, repeated separation and loss, excessive demands from authority figures, or various organic insults.

In discussing the environmental variables and their impact on a constitutionally vulnerable child, Anthony has noted the effects of the ill parent on the child in a detailed description of parent-child interactions. In his study of the children of psychotic parents, Anthony observed that the sicker schizophrenic parents (diagnosed hebephrenic or catatonic) produced healthier children, while the relatively healthier parents (diagnosed schizoid or borderline) produced more deviant children. He took into consideration the age of the child at the time of the mother's illness and the family support system in terms of other available members with whom the child could identify or become involved. He felt that the most disturbed children were

those symbiotically involved with the ill parent and that children under two, still in the phase of separation-individuation, were especially sensitive to the disturbing influence of the chronically ill mother. Whether the child internalizes or externalizes conflict, how compliant or negativistic he is, how prone to a *folie-a-deux,* and how identified with the ill parent, determine his ultimate development. Anthony observed that the more disturbed children suffered a loss of ego-skills by school age and exhibited symptoms such as nightmares, phobias, obsessions, or antisocial behavior. In a similar vein, Kauffman and associates found:

> that the mother's current level of functioning is even more important than the diagnosis of her condition in understanding the impact of her disturbance on the child's later development. Women who are isolated from social contacts and who cannot function effectively in their adult social roles have children with lower competence . . . [p. 1401]

Thus, environmental influences, particularly paucity of supports, produced less competent children.

Research in Early Identification of Schizophrenia

The four methods used for studying the premorbid history are:

1. clinical retrospective (reports of life history, patient or family reminiscences)

2. follow-back study (case records of adult schizophrenics traced back

to childhood)

3. follow-up study (life history of the child at-risk who was evaluated in childhood and reevaluated as an adult)

4. prospective longitudinal study (a high-risk group followed into adult life so that incipient pathology may be studied in depth)

The last method has the obvious advantage of a carefully designed methodology and permits the researcher greater objectivity by reliance on a matched control sample, double-blind ratings, and the passage of time.

Impressionistic data derived by the other three methods, however, produced hypotheses about the premorbid state which could then be tested by the prospective longitudinal method.

Example of the Follow-Back Study Method

Watt, in a controlled study, examined past cumulative school records of fifty-four hospitalized schizophrenic adults. He found that over one-third were identified by teachers as being deviant in childhood before they showed psychotic disorganization. Patterns of maladjustment for boys and girls differed.

Pre-schizophrenic boys exhibited primary evidence of unsocialized

aggression and secondary evidence of internal conflict, over-inhibition, and depression. Pre-schizophrenic girls exhibited primary evidence of oversensitivity, conformity, and introversion.

Watt found that both sexes had been subjected to heightened frequency of parental deaths and neurological abnormalities compared to controls. He proposed five postdictive indices of schizophrenia: (1) parental death; (2) severe organic handicap; (3) extreme emotional instability; (4) extreme introversion (females); and (5) extreme disagreeableness (males). In a subsequent study, low social competence was associated with withdrawal, thought disorder, and antisocial acting out.

Example of the Follow-up Study Method

Waring and Ricks, using the follow-up method, identified 75 adult schizophrenics selected from the records of 18,000 children seen in a child guidance clinic since 1917. Subjects were divided into two groups: chronic (those whose illness did not remit) and released (those who had been hospitalized intermittently for schizophrenic illness). Differences between schizophrenic patients and normal controls were: (1) developmental history —fewer than 40 percent had normal births; (2) early neurological dysfunction (slower motor development, poorer coordination, unclear speech); and (3) absence of heterosexual experience or extreme homosexual

fears during childhood.

Differences between the two groups were also noted. As compared to the released group, the chronic schizophrenics were characterized by: (1) family history of schizophrenia; (2) mothers who were more disturbed (psychotic or functioning on a borderline level); (3) a symbiotic relationship with the ill mother; (4) a schizoid premorbid personality with few close peer relationships; (5) no clear precipitating event necessitating hospitalization; and (6) no history of sociopathy, (truancy, stealing).

Ricks and Berry, discussing children who become schizophrenic, maintained that chronic schizophrenics have biological and social equipment that offers small margin for error in development, and their coping mechanisms are clearly maladaptive. The investigators feel that the IQ, degree of social and vocational success, the home environment, and the presence or absence of biological handicap are all relevant.

The Prospective-Longitudinal Method of High-Risk Research

Pearson and Kley were the first investigators to propose a prospective study of individuals at high statistical risk for schizophrenia. In 1959, non-blind studies were instituted by B. Fish, who subsequently followed up infants born to schizophrenic mothers, and Sobel, who attempted to study infants of two schizophrenic parents. “Pan developmental retardation,” Fish suggested,

is a transient dysregulation of motor, visual-motor, and physical development noted between birth and two years; this includes erratic and disorganized maturational patterns in activity and alertness, as well as autonomic instability, which, Fish believes, predict vulnerability to later schizophrenia.

In 1962 Mednick and Schulsinger, using more sophisticated methodology, began a longitudinal study of Danish children of schizophrenic mothers. The investigators believed that the offspring of schizophrenic mothers demonstrated a particular vulnerability to schizophrenia that is a joint function of genetic loading and pregnancy and birth complications. This combined liability, they contended, results in an infant who demonstrates a labile pattern of autonomic responsivity.

Neurological "Soft Signs"

There is still controversy about some of the recorded physiological data (i.e. regarding differences in galvanic skin responses between high-risk subjects and normal controls), but there is high agreement among investigators as to the neurological soft signs noted in the offspring of schizophrenics. Such findings have been reported in many studies. Marcus, in a study undertaken in Israel in 1965, identified a group of offspring born to schizophrenic parents. The children were characterized by soft signs of neurological dysfunction, (deficits in fine motor development, visual-motor

coordination, and auditory-visual integration). The finding suggested to Marcus a genetic basis for vulnerability to schizophrenia. In a second study, Marcus and associates were able to identify a subgroup of infants born to schizophrenics who demonstrated the same dysmaturation in motor functions as in perceptual development. The investigators, using a Multidimensional Scalogram Analysis, found that roughly one-half of the high-risk infants exhibited less than optimal functioning. They noted, moreover, lower birth weights in these infants as compared to controls and the other group of high-risk infants whose functioning was optimal. In a subsequent study, Marcus and Mednick examined the data on a subsample of the Danish high-risk, birth-matched subjects and reanalyzed them using a Multidimensional Scalogram Analysis.

When area judgment scores were reexamined, approximately half of the high-risk children could be identified by the repeated findings of less than optimal functioning in motor and coordination tasks, posture, and gait.

Obstetrical Complications

Mednick's original high-risk study demonstrated that the clinically deviant group of adolescent offspring had had a significant increase in anomalous autonomic responses and high rates of obstetrical complications. McNeil and Kaij, in reviewing over eighty papers relating to obstetrical factors

in the development of schizophrenia, observed that the outcome of these studies demonstrated few significant differences between the high-risk subjects and their controls in overall obstetrical complications— pregnancy complications (PC), birth complications (BC), neonatal complications (NC), and obstetrical complications (OC).[2] Two of the studies however, showed significantly more fetal and neonatal deaths in index pregnancies; the 1978 report by McNeil and Kaij of a Swedish high-risk sample, revealed increased NC's and OC's corroborating Mednick's 1970 study. Low birth weight was reported in three studies. Marcuse and Cornblatt, in a review of current findings of OC's in relation to soft signs, noted that the relationship between neurological signs in high-risk children is currently unresolved. In their investigation of the relationship between OC's and neurological outcome in a sample of children with schizophrenic parents, they reviewed information in preliminary analysis data on seventeen high-risk children and sixty-eight matched controls. The index cases were selected from the Collaborative Perinatal Project, which recorded obstetrical information on 55,000 pregnancies with follow-up from birth through age five. Positive findings were: (1) male high-risk children had more NC's and total OC's than control cases or high-risk females (The two NC items individually significant were prematurity and low one-minute Apgar scores); and (2) the high-risk group was markedly deficient in the Auditory-Vocal Association Test, block sorting, and school achievement (IQ was a controlled variable). The investigators

noted that there was a subgroup of individuals who scored poorly on both OC's and neurological variables, and who had at least one obstetrical indicator and abnormal neurological signs (that is, poor coordination, short attention span, mixed dominance, and other anomalies of lateral dominance). Marcuse and Cornblatt noted that "the consistency of the neurological findings across studies is quite remarkable. Nearly every attempt to examine motor functions and soft signs has demonstrated statistical group differences or associative patterns that distinguish the offspring of schizophrenics from controls."

In another carefully controlled prospective study, Hanson and associates collected developmental data on thirty-three children of schizophrenic parents from the Collaborative Perinatal Project, Minnesota Sample. Matched control groups consisted of children of other psychiatric patients and normal parents. Seventeen percent of the high-risk sample had positive scores on the three following indicators: poor motor abilities, schizoid behavior, and marked inconsistencies in academic cognitive achievement. While some of the controls provided positive findings on one or two indices, none provided positive scores on all three. The authors concluded that these specific individuals were especially vulnerable to schizophrenia.

Example of a High-Risk Prospective Study

One of the most extensive of the high-risk prospective studies has been in progress since 1971 at the New York State Psychiatric Institute, where the chief investigator is L. Erlenmeyer-Kimling. The risk group includes 205 children who were between the ages of seven and twelve at the time of initial examination (sample A). The 80 high-risk subjects are subdivided into three groups: 44 with schizophrenic mothers, 23 with schizophrenic fathers, and 13 with two schizophrenic parents. The two control groups consist of 25 children of parents with another psychiatric disorder and 100 children whose families do not have psychiatric disorders. The index cases are matched for age, sex, ethnicity, and social class. Strict diagnostic criteria were used in selecting the parents. The chief focus of the study is on psychophysiological, psychiatric, neurological, psychological, and social measures. According to hypotheses based on research with adult schizophrenics, which postulate that schizophrenic individuals may have difficulty in normal processing of stimuli, measures were selected that would be expected to be deviant in pre-schizophrenic individuals.

Tests were selected that measure attentional dysfunction and distractibility. It was felt that genetically vulnerable individuals may have difficulty in "filtering out" background stimuli or may be unable to disengage from a stimulus having once attended to it.

The subjects are given home interviews and laboratory testing that

include structured and semi-structured interviews, neurological examination, and psychological tests such as the Wechsler Intelligence Test, Bender-Gestalt, Human Figure Drawing, and projective tests. School records are collected; a variety of cognitive, attentional and distractibility measurements are administered, as well as EEG and auditory evoked potentials. A videotaped psychiatric interview using a semi-structured interview—the Mental Health Assessment Form—was developed for the project. The interviewer is "blind" as to the child's parental background, as are three raters who independently rate the videotapes for psychopathology and diagnostic impressions. A second group under investigation consisting of 150 subjects, (sample B) has been included as a replication sample (44 children of one or two schizophrenic parents, 40 whose parents have affective disorders, and 66 with normal parents).

Preliminary Results of Group Differences

In addition to corroboration of positive neurological findings in the index cases consistent with those of other investigators, a study of attentional tasks has emerged that differentiates the high-risk group from the controls. The first sample (sample A) has been tested on three occasions over a nine-year period. Consistent group differences were found on several attentional measures, the Continuous Performance Test (CPT)[3] and the Attention Span Measure, which requires subjects to recall immediately a series of either three

or five letters presented by tape recorder, with or without distraction.

The results on the CPT indicated that the high-risk subjects made significantly fewer correct responses and significantly more random commission errors than did the normal comparison group, with and without distraction. On the Attention Span Measure, high-risk subjects also made significantly fewer correct responses than the normal comparison groups under certain conditions.

Neuropsychological and Neurophysiological Measures

The high-risk subjects scored lower on the tests of neuropsychological development (Bender-Gestalt and Human Figure Drawing Test). The finding suggested a developmental lag as described by B. Fish. Some of these subjects showed unusual patterns of auditory-evoked potentials, particularly when attention was required as a task.

Current Clinical Status

In a preliminary analysis of differences between the index and control children using the videotaped Mental Health Assessment Form, there were significant differences on global assessment of function, anxiety, depression, history of angry feelings, disturbance in relationship with the mother, occurrence of nightmares, and measures of self-esteem.

Deviant Cognitive Performance-Deviant-Behavior Overlap

Behavioral disturbances were measured according to a five point Behavioral-Global Adjustment Scale that relies heavily on parents' information. "The subgroup identified as deviant within the high-risk group has been found to show an increasing overlap with the subjects showing behavioral problems as they reach adolescence."

Teachers' reports also showed the high-risk subgroup having increasing school difficulty when these children entered adolescence. The current clinical status of the study children, whose mean age is fifteen years, reveals that to date eight subjects of the original 205 (4 percent) have been hospitalized or treated for serious disorders. Five of the eight hospitalized children are from the high-risk group, two are from the psychiatric comparison group, and one from the normal comparison group. All but the child from the normal comparison group had demonstrated dysfunction in the CPT and other attentional measures several years prior to breakdown.

Summary of Findings

The study thus far points to the presence of neurological soft signs in the high-risk group in early childhood. Attentional and cognitive measures as well as attention-related auditory-evoked potentials appear to discriminate between a subgroup of high-risk and control subjects at early ages. These

measures are associated with clinical deviance in adolescence, noted by parents, by teachers, and global assessment. The fact that the children with early deficits on laboratory measures become increasingly deviant behaviorally as they get older supports the hypothesis that attentional dysfunctions serve as early predictors of later pathology.

Case Illustration[4]

Mona, the only child of a middle-aged couple, was referred for psychiatric treatment at age six by her school principal because of extreme shyness, school refusal, inconsistent work habits, and "joylessness." Additional symptoms reported by her parents were: frequent nocturnal, and occasionally diurnal, enuresis; multiple fears (of animals, of the dark, and of being alone); belief in "supernatural powers" (for example, she was convinced that the eyes in photographs or paintings followed her around the room).

Early manifestations of deviance (her mother's pregnancy and delivery having been normal) were hypersensitivity to noise and change (new faces or surroundings), and more-than-expectable separation anxiety. Food "fads" and rejection of all but five or six foods were reported along with a preoccupation with thoughts of vomiting (which had occurred on occasion during febrile illnesses).

Significant traumatic events when Mona was four were the

simultaneous death of her grandmother and a month-long hospitalization of her mother for an operable malignancy.

Family history: Mr. S. was a psychiatrically well, successful businessman, "obsessional and quiet," by his own report. Mrs. S. had a history of emotional problems. Her father was alcoholic, suspicious, physically abusive, unable to keep steady employment, and was known in his family as "the crazy one." Never hospitalized for psychiatric illness, he had a brother who died in a mental institution. Mrs. S. left home at age sixteen and worked as a secretary until her marriage at age thirty-five. A "loner," she was in treatment for agoraphobia, which was so incapacitating at times that she could not attend her psychiatric sessions. She had the habit of sending the therapist many pages of "associations" (described as loose and rambling) in lieu of sessions.

Evaluation

Because of Mona's "staring spells," a neurological examination was performed. Results were within normal limits.

A psychological examination revealed a full scale IQ of 115 (WISC) "with higher potential" and subtest scatter (lowered scores for language comprehension and picture arrangement). Language structural skills were poor. Projective tests were characterized by "peculiar percepts: monsters, dragons, skeletons, eyes. . . . Suspicious, phobic, and much like an adult

diagnosed paranoid personality," reported the psychologist.

Therapeutic Course

During the initial biweekly psychotherapy sessions, Mona avoided eye contact. Themes of her drawings included fire, explosion, death, and destruction. A well-executed drawing of a smiling girl brought forth the comment, "She's happy because she's eavesdropping on her enemies. Everything about this girl is bad; she has no friends, she is mean, and she hates everyone".

The initial mode of therapy was doll play. Mona reenacted with the dolls events she would not describe in words, giving detailed accounts of what the dolls thought and felt. For example, doll A explained to doll B, "It's dangerous to eat something you don't like; then you'll vomit and your head will fall off and your stomach will burst." Mona was convinced eyes had special controlling powers and thoughts could kill.

Initial therapeutic intervention was in the nature of establishing trust, the therapist serving as a reality-organ, correcting Mona's distortions and, whenever possible, offering interpretations. The parents were counseled not to comply with Mona's every command —for example, to remove the pictures from the wall or allow her to remain home from school. The teachers had a direct line to the therapist as well and instituted special educational therapy

to help Mona develop language skills and powers of concentration.

As Mona developed more confidence, she acquired several friends and joined the girl scouts clubs. In therapy, new themes continued to emerge involving her low self-esteem, confused body image, and maladaptive defense mechanisms, chiefly denial and projection. When Mona was eight for example, she enacted the role of eight-year-old Moira "who was born two months ago —she didn't want to come out of her mother's tummy; she has two brains; one which turns itself off when she wants to go into her secret world."

The therapist helped Mona work through her feelings of being "queer," or different from other children, and helped her find better ways of solving problems. In preadolescence, Mona became deeply upset by her budding sexuality. Her thoughts became confused and she experienced episodes of depersonalization.

The bizarre quality of her imagination and fear of pubertal change and bodily damage was exemplified by one of her stories when she was twelve years old: "Moira was bad, went to jail, got pregnant, and had an abortion. She stuck the [fetus] back into her vagina to grow again, but instead, Moira turned herself inside out, upside down, and her ovaries started to walk on two little tube-like legs. She cried, but instead of tears falling, little eggs dropped out."

The therapist again served as "the voice of reality," correcting

distortions, and encouraging Mona to use her verbal expressiveness to create stories that could more appropriately be shared with teachers and schoolmates. Mona became editor of the school paper and achieved success and won admiration from her peers for her writing skills. Treatment was terminated at age fourteen when Mona's family moved out of state.

Ten-year follow-up revealed that Mona had made a good adjustment to college life (in a small non-pressured college), and had selected several male teachers as "mentors" to guide her in her literary interests and writing skills. She had one or two friends and found employment as a school librarian. A psychiatric consultant considered her diagnosis to be "schizoid personality" or "schizotypal personality disorder" since she met all the eight inclusion criteria.[5] The question as yet unanswered is: what part did early intervention play in preventing a schizophrenic breakdown in a vulnerable individual?

The Child at Risk for Manic-Depressive Psychosis: Historical Review and Risk Data

Kraepelin, in 1896, classified manic-depressive psychosis as a unitary form of mental illness distinct from schizophrenia. He noted, in his 1921 monograph, that the strength of the hereditary factor was 75 percent, that 70 percent of his cases were women, and that 25 percent of his manic-depressive patients were alcoholics. According to Rosenthal, there is a high rate of lifetime prevalence of affective disorders in the first and second degree

relatives of patients with primary affective disorders as compared with the general population (6 to 24 percent versus 1 to 2 percent). Bipolar manic-depressive psychosis occurs in 0.5 percent of the population as contrasted with the 0.85 to 1.5 percent worldwide incidence of schizophrenia. Risk figures for manic-depressives psychosis in the first degree relatives of manic-depressive index cases from eleven studies from 1921 to 1953 are the following: parents 7.8 percent; siblings 8.8 percent; children 11.2 percent.

A genetic hypothesis has been supported by Zerbin-Rudin in a review of six major studies of twins. Overall concordance rates for monozygotic twins were consistently higher than for dizygotic twins (74 percent versus 19 percent).

Employing strict diagnostic criteria, Bertelsen and associates studied sixty-nine monozygotic probands and determined that the concordance rate was 67 percent versus the corresponding dizygotic twin concordance of 20 percent. (The difference is significant at $p < 0.001$.) A rare case of monozygotic twins reared apart who were concordant for manic-depressive illness was reported by Rosanoff and associates in 1935, and the data reanalyzed by Farber in 1979.

Cadoret found that the incidence of depression was significantly higher in the affect-disordered parent adoptees than in adoptees whose biological

parents had other psychiatric conditions or were apparently psychiatrically well. Findings of Mendlewicz and Rainer point to a similar conclusion. Psychopathology in the biological parents was in excess of that found in the adoptive parents of the same manic-depressive offspring.

Case Illustration

Marcy, a fourteen-year-old girl was suspended from school for truancy and marijuana intoxication. Considered "wild" by parents and teachers, she was subject to intense mood swings. Popular with girls and boys, she had several close friends and did well academically until seventh grade when school performance became inconsistent.

Family background was positive for affective disorder on both sides. The chronically depressed maternal grandfather had been hospitalized once and received electroconvulsive therapy (ECT). The mother, an explosive, volatile woman, had been treated for depression with psychotherapy and antidepressant medication for many years. One of her brothers had undergone repeated hospitalizations for alcoholism, antisocial behavior, and suicide attempts. The father, psychiatrically stable, had a sister who committed suicide at age twenty-five following psychiatric hospitalization for a "nervous breakdown" (diagnosis uncertain). Marcy's sixteen-year-old brother had been hyperactive in childhood and had been expelled from school

in early adolescence for stealing from classmates and vandalism.

Psychological tests revealed a 14 point discrepancy between the verbal and performance WISC (114 versus 100). The lower performance score was due to inattentiveness to objective detail on the picture completion test and coding. Projective tests revealed a projective tendency, distrust of authority figures, rage, and an underlying depressive trend.

Psychotherapy was refused. Because of temper tantrums and impulse dyscontrol, Marcy was sent to a boarding school known for its therapeutic milieu. The staff reported extreme lability of mood; she would shift from ebullience to despair within hours. Her dreams were frightening or gloomy ("I dreamed I was dead, I went to my own funeral and saw myself lying in a coffin"). At other times she was overexcited and verbose.

Marcy remained in the school two years. The staff reported that at sixteen Marcy's school work began to deteriorate. Marcy became sexually promiscuous, refused to obey school rules, was often truant, and explosive rage reactions became more frequent. She ran away from school, having stolen a car.

Grossly delusional, she was convinced she was about to become a famous Hollywood singer.

A psychiatric consultant recommended hospitalization for manic-depressive psychosis with appropriate medication and psychotherapy following the hospital course.

Discussion

Current research concerning the precursors of schizophrenia and affective disorder is still in its infancy, yet a number of factors are becoming apparent. Certain symptom clusters in genetically predisposed individuals may be predictive of future illness. Specific differences in symptomatology together with a family history positive for either schizophrenia or affective disorder may help in identifying the underlying disturbance.

The case of Mona, for example, demonstrates many of the features noted in children at risk for schizophrenia: positive family history, early signs of hypersensitivity, traumatic separations, illness and death of relatives, and an emotionally labile mother. Investigators have described symptom clusters similar to hers in children who became schizophrenic in adult life (extreme shyness and introversion, magical thinking not commensurate with age or intelligence, anhedonia, phobias, attentional problems, and maladaptive defense mechanisms such as projection and denial). Mona exhibited failure of repression and a tendency toward regression reminiscent of the children described by Ekstein and Wright, and Kestenbaum.

The case of Marcy, an example of adolescent manic-depressive disorder, is illustrative in that different symptom clusters are in evidence. The family history of affective disorder and Marcy's early history of temper tantrums, impulsivity, lowered frustration tolerance and dysphoria, behavior problems and lack of judgment point to a manic-depressive diathesis.

An interesting psychometric finding, in contrast to Mona's IQ differential, was Marcy's superior verbal IQ and significantly lower performance scores on the WISC—a finding noted in Anthony's 1960 case report. Low scores on the visuo-constructive tests are reminiscent of the scores obtained by children with certain types of minimal brain damage, according to Gardner. Appreciation of spatial relationships is considered to be primarily a function of the right cerebral hemisphere as is the processing of complex nonverbal sensory input. Right hemispheric dysfunction might explain the inability to perform well on block design, picture arrangement, picture completion, object assembly, and mazes subtests.

Certain investigators have postulated that individuals who have a family history positive for manic-depressive illness may have a greater right than left hemisphere deficit. Moreover, they may have a high incidence of disinhibition syndrome which could be the result of subtle frontal brain systems dysfunction, similar to that which characterizes hyperkinetic disorder.

Flor-Henry has formulated a similar hypothesis for adults with manic-depressive disorder. The findings suggest the possibility of a fundamental genetic liability—the lack of some central inhibitory regulating mechanism—that may lead to a manic-depressive illness in later life. This observation is in contrast to the possibility of left-hemispheric dysfunction in schizophrenics, which has been reported in recent neurophysiological investigations. At this time, controlled studies are sparse and further investigation is required for better understanding of the neurophysiological basis of mental functioning.

Anthony and Scott, in a review of the literature from 1896 to 1960, concluded that manic-depressive illness in childhood is extremely rare. They contend that the early variety may be due to heavy genetic loading and intense environmental experience, that it may be manifested during childhood under strong physical or psychological pressure, and that it may, under certain circumstances, become clinically recognized as a psychosis. Youngerman and Canino reviewed 190 cases of lithium carbonate in children and adolescents and noted that "many adolescent manic-depressives have histories of behavior and mood disorders often dating back to early childhood. Affective symptoms are mixed and masked in childhood, and it is difficult to elicit reports of sustained mood swings" [p. 223].

Other investigators have described children with a family history positive for bipolar illness, and various symptom complexes including sleep

disorder, night terrors, rage attacks, grandiosity, and socially inappropriate behavior. Davis has proposed that there is an identifiable syndrome, which he calls manic-depressive variant syndrome of childhood (MDV), characterized by positive family history of affective disturbance, hyperactivity, temper tantrums, and impairment in personal relationships.

Possible Predictors of Future Affective Disorders

There are few prospective studies as yet of children at high risk for affective disorder. Several studies demonstrate that a significant number of patients hospitalized for depression were parents of children who exhibited episodes of depression. There are relatively few studies, however, of the children of bipolar manic-depressive parents. Clinical descriptions from actual examination rather than from parents reports together with psychological test scores are sparse. Kestenbaum has described thirteen children with a family history of bipolar manic-depressive disorder; six of the children (four males, two females) exhibited the following features:

1. Family history positive for bipolar illness;

2. Specific clinical symptomatology including temper tantrums, compulsive rituals, dysphoria, lability, obsessional preoccupation, learning disability, hyperactivity, impulsivity;

3. Specific patterns in psychological test scores (WISC) revealing

verbal achievement significantly greater than performance, with considerable subtest scatter.

Of the remaining seven, three (all females) had psychological test scores that did not follow the pattern described above; four (two males, two females) were not given psychological tests. The presenting symptoms of these seven children were depressed mood (N = 5) and behavior problems (N = 2). The presenting symptoms of the six children exhibiting the triad of features of the triad mentioned above were learning problems with depressed mood (N = 5) and hyperactivity with behavior problems (N=1) [p. 1207].

Genetic Themes of Transmission

Genetic and clinical variables have been noted which differentiate bipolar from unipolar illness. Bipolar probands were observed to have a higher suicide rate, earlier age of onset, and peptic ulcers in greater numbers than unipolar probands. Bipolar females demonstrated heightened vulnerability to postpartum psychosis. Unipolar disorders tend to begin later (forty-three versus thirty-one years), are more frequently females, and are less severe. Winokur has suggested that depressive disorder be divided into autonomous subtypes based on family history: (1) depressive spectrum disease in an individual with a first degree history of alcoholism or antisocial personality; and (2) pure depressive illness in an individual without similarly affected relatives. Thus, family studies have led some investigators to

conclude that unipolar and bipolar illnesses are genetically different entities. Theories of genetic transmission of affective disorders postulate: (1) autosomal dominance; (2) genetic heterogeneity; (3) X-linked gene associated with red, green colorblindness and Xga blood type; and (4) multiple threshold models. (A variable liability to a disorder is postulated to which genetic and independent factors may contribute. If the net liability crosses a certain threshold, the disorder becomes manifest). Gershon suggested that unipolar and bipolar illnesses represent positions on a continuum of liability.

Greater liability would tend to manifest itself as bipolar illness, lesser liability as a unipolar disorder. Along with Dunner and Goodwin, Gershon contended that the individual with a manic-depressive illness has "an inherited vulnerability to loss, with increased likelihood of development of pathological loss reactions" [p. 8].

Juvenile Manic-Depressive Illness

Serious forms of depression are commonly encountered in childhood.' Symptoms include sad affect, social withdrawal, psychomotor retardation, anxiety, school failure, sleep disturbance, feelings of hopelessness and helplessness, suicidal preoccupation, and self-deprecatory ideation. All of the investigators noted that while depressive symptoms are common, mania in childhood is extremely rare. Recent genetic studies, however, have

demonstrated that a first episode of bipolar illness in adolescence is not uncommon. Winokur and associates noted that one-third of their bipolar cases had a first episode occurring between ten and nineteen years of age. Nonetheless, manic episodes in adolescence are frequently misdiagnosed. Carlson and Strober described six cases of adolescents initially diagnosed as schizophrenics who were, at a later admission, re-diagnosed manic-depressive. Stone also described the present tendency to label young patients "schizophrenic until proven otherwise" [p. 16].

Conclusion: Prevention and Intervention

Hypotheses about the environmental variables that interact with constitutional factors in the development of schizophrenia or affective disorders include neurophysiological dysfunctions, which can be tested in a laboratory, as well as family interaction patterns and coping skills, which are currently being examined by accurate measurements outside the laboratory. Pooling data from different research projects provides a massive amount of information about the at-risk children so that it should become easier, in time, to isolate those variables that predict eventual breakdown.

Interventions are particularly useful when they are specifically directed toward correcting primary problems. Until more is known about the core psychopathology involved in the major psychoses, primary prevention and

therapeutic interventions involve much guesswork.

The evidence gathered thus far indicates that the pre-schizophrenic child has difficulty filtering stimulus input and has problems in attention that subsequently lead to school difficulties and social problems. The pre-manic-depressive child may exhibit difficulty with impulse control and regulation of moods as well as with other subtle manifestations of nonverbal learning disability.

Early intervention should include genetic counseling, careful perinatal examination, and frequent pediatric developmental evaluation of at-risk children, with particular focus on language delay. Therapeutic nurseries and language-and-learning therapies might be made available to children who showed signs of early deviance.

> The at-risk child who is "bright but not living up to his potential" should be evaluated as soon as symptoms appear; school failure, attentional problems, social withdrawal, loss of self-esteem should not be left unnoticed until symptoms become fixed. . . . Special school programs for the child with attentional problems should focus on strengthening existing assets which would enhance self-esteem. [p. 174]

Recommendations for family treatment, selection of a proper school or camp, and individual psychotherapy or pharmacotherapy might be made to fit the particular needs of each family. Such environmental interventions may not prevent a psychotic breakdown in adult life, but the coping mechanisms

acquired by such intervention techniques may shorten the course of the illness.

An interesting outcome of Anthony's study was his discovery that some of the children of schizophrenic parents (5 to 10 percent) reacted with super-normality, tolerating the family problems with equanimity. These so-called "invulnerable" children demonstrated unusual talents and coping abilities. Other investigators have described such "super-kids" who have emerged from sick families as having a wide variety of interests and unusual capabilities. Most of the children were from the schizophrenic group and had mothers who, despite their illness, were warm and supportive. Depressed mothers, unable to respond to their infants' needs, seem to have a more profoundly negative impact on their children. One must assume that an invulnerable child in a sick family is one who is constitutionally better equipped to cope with stress than his less fortunate siblings and who, in addition, has access to beneficial environmental support systems.

The study of children at risk is producing new information about mental illness *in statu nascendi.* Understanding the process involved may provide basic solutions to one of mankind's most pervasive problems.

Bibliography

Altshuler, K. Z. "Deafness and Schizophrenia: Interrelation of Communication Stress, Maturation

Lag, and Schizophrenic Risk," in Kallmann, F. J., et al., eds., *Expanding Goals of Genetics in Psychiatry.* New York: Grune & Stratton, 1962, pp. 52-62.

Annell, A. "Lithium in the Treatment of Children and Adolescents," *Acta Psychiatrica Scandinavica, Suppl.* 207 (1969): 19-30.

Anthony, E. J. "A Clinical Evaluation of Children with Psychotic Parents," *American Journal of Psychiatry,* 126:2 (1969): 177-184.

Anthony, E. J., and Scott P. "Manic-Depressive Psychosis in Childhood," *Journal of Child Psychology and Psychiatry,* 1 (1960): 53-72.

Arieti, S. *Interpretation of Schizophrenia.* 2nd ed., New York: Basic Books, 1974.

Bateson, G., et al., "Toward a Theory of Schizophrenia," *Behavioral Science.* 1 (i95) 251-264.

Bemporard, B. "Children of Manic-Depressives," unpublished Ph.D. diss., Columbia University, forthcoming.

Berg, I., et al. "Bipolar Manic-Depressive Illness in Early Adolescence. A Case Report," *British Journal of Psychiatry,* 125 (1974): 416-417.

Bertelsen, A., Harvald, B., and Hauge, M. "A Danish Twin-Study of Manic Depressive Disorder," *British Journal of Psychiatry,* 130 (1977): 330-357.

Bleuler, E. *Dementia Praecox or The Group of Schizophrenias.* New York: International Universities Press, 1950.

Buchsbaum, M. "Average Evoked Response Augmenting/Reducing in Schizophrenia and Affective Disorder," in Freedman, D.X., ed., *Biology of the Major Psychoses.* New York: Raven Press, 1975, pp. 129-142.

Cadoret, R. J. "Evidence for Genetic Inheritance of Primary Affective Disorder in Adoptees," *Americal Journal of Psychiatry,* 17:1 (1978): 138-153.

Cadoret, R. J., and Winokur, G. "X-Linkage in Manic-Depressive Illness," *American Review of*

Medicine, 26 (1975): 21-25.

Carlson, G. A., and Strober, M. "Manic-Depressive Illness in Early Adolescence," *Journal of American Academy of Child Psychiatry,* 17 (1978): 138-153.

Chapman, J., and McGhie, A. "A Comparative Study of Disordered Attention in Schizophrenia," *Journal of Mental Science,* 108 (1962): 487-500.

Cornblatt, B., and Marcuse, Y. "Children at High-Risk for Schizophrenia: From Childhood to Adolescence," in Erlenmeyer-Kimling, L., Dohrenwend, B. S., and Miller, N., eds., *Life Span Research on the Prediction of Psychopathology,* forthcoming.

Cytryn, L., and McKnew, D. H. J. "Proposed Classification of Childhood Depression," *American Journal of Psychiatry,* 129 (1972): 149-155.

Davidson, K., and Bagley, C. R. "Schizophrenia-like Psychoses Associated with Organic Disorders of the Central Nervous System: A Preview of the Literature," *British Journal of Psychology, Special Publication* no. 4, ("Current Problems in Neuropsychiatry"), 1969 p. 113.

Davis, R. E. "Manic-Depressive Variant Syndrome of Childhood (The M.D.V. Syndrome, A Preliminary Report," *American Journal of Psychiatry,* 136:5 (1979): 702-705.

Dince, P. R. "Maternal Depression and Failures of Individuation During Adolescence," in Musserman, J., ed., *Science and Psychoanalysis,* New York: Grune & Stratton, 1966, pp. 26-37.

Dyson, W. L., and Barcai, A. "Treatment of Children of Lithium-Responding Parents," *Current Therapeutic Research— Clinical and Experimental,* 12 (1970): 286-290.

Ekstein, R., and Wright, D. C. "The Space Child," *Bulletin of the Menninger Clinic,* 16 (1952): 211-224.

Erlenmeyer-Kimling, L. "Studies on the Offspring of Two Schizophrenic Parents," in Rosenthal, D. and Kety, S. S., eds., *The Transmission of Schizophrenia.* New York: Pergamon Press, 1968, pp. 65-83.

----. “A Prospective Study of Children At-Risk for Schizophrenia: Methodological Considerations and Some Preliminary Findings,” in Wirt, R. D., Winokur, G., and Roff, M., eds, *Life History Research in Psychopathology.* vol. 4, Minneapolis: University of Minnesota Press, 1976, pp. 22-46.

----. “Issues Pertaining to Prevention and Intervention in Genetic Disorders Affecting Human Behavior,” in Albee, G. W. and Joffe, J. M., eds., *Primary Prevention in Psychopathology*. Hanover, N.H.: University Press of New England, 1977, pp. 68-91.

----. “Genetic Approaches to the Study of Schizophrenia: The Genetic Evidence as a Tool in Research,” *Birth Defects* (Original Article Series), 14:5 (1978): 59-74.

Erlenmeyer Kimling, L., and Paradowski, W. “Selection and Schizophrenia,” in Bajema, C. J., ed., *Natural Selection in Human Populations.* New York: John Wiley, 1971, pp. 651-665.

Erlenmeyer Kimling, L., Cornblatt, B., and Fleiss, J. “High-Risk Research in Schizophrenia,” *Psychiatric Annals*, 9(1) (1979): 38-51.

Farber, S. *Identical Twins Reared Apart.* New York: Basic Books, 1981.

Feinstein, S., and Wolpert, E. A. “Juvenile Manic-Depressive Illness Clinical and Therapeutic Considerations,” *Journal of American Academy of Child Psychiatry,* 12 (1973): 123-136.

Fish, B. “Abnormal States of Consciousness and Muscle Tone in Infants Born to Schizophrenic Mothers,” *American Journal of Psychiatry,* 119 (1962): 439-445.

----. “Biologic Antecedents of Psychosis in Children,” in Freedman, D.X., ed., *Biology of the Major Psychoses,* vol. 54, New York: Raven Press, 1975, pp. 49-80.

Flor-Henry, P. “On Certain Aspects of the Localization of the Cerebral Systems Regulating and Determining Emotions,” *Biological Psychiatry,* 14:4 (1979): 666-697.

Friedman, D., Vaughan, H., and Erlenmeyer-Kimling, L. “Stimulus and Response Related Components of the Late Positive Complex in Visual Discrimination Tasks,” *Electroencephalography and Clinical Neurophysiology,* 45 (1978): 319-330.

Gardner, R. A. *The Objective Diagnosis of Minimal Brain Dysfunction.* Cresskill, N.J.: Creative Therapeutics, 1979.

Garmezy, N. "Children-at-Risk: The Search for The Antecedents of Schizophrenia, Part 1: Conceptual Models and Research Methods," *Schizophrenia Bulletin,* 8 (1974): 14-90.

Gazzaniga, M. S. *The Bisected Brain.* New York: Appleton-Century-Crofts, 1970.

Gershon, E. S., Dunner, D. L., and Goodwin, F. K. "Toward a Biology of Affective Disorders," *Archives of General Psychiatry,* 25 (1971): 1-15.

Gottesman, I.I. "Schizophrenia and Genetics: Toward Understanding Under-tainty," *Psychiatric Annals,* 9 (1) (1979): 26-37.

Gottesman, I. I., and Shields, J. *Schizophrenia and Genetics: A Twin Study Vantage Point.* New York: Academic Press, 1972.

Grinker, R. R. Sr., and Holzman, P. S. "Schizophrenic Pathology in Young Adults," *Archives of General Psychiatry* 28 (1973): 168-175.

Hanson, D. R., Gottesman, 1.1., and Heston, L. L. "Some Possible Childhood Indicators of Adult Schizophrenia Inferred from Children of Schizophrenics," *British Journal of Psychiatry,* 129 (1976): 142-154.

Heston, L. L. "Psychiatric Disorders in Foster Home Reared Children of Schizophrenic Mothers," *British Journal of Psychiatry,* 112 (1966): 819-825.

Kallmann, F. J. *The Genetics of Schizophrenia.* Locust Valley, New York: J. J. Augustin, 1938.

----. "The Genetic Theory of Schizophrenia: An Analysis of 691 Schizophrenic Twin Index Families," *American Journal of Psychiatry.* 103 (1946): 309-322.

Kauffman, C., et al. "Superkids: Competent Children of Psychotic Mothers," *American Journal of Psychiatry,* 136:11 (1979): 1398-1402.

Kestenbaum, C. J. "Psychotherapy of Childhood Schizophrenia," in Wolman, B., Egan, J., and Ross,

A., eds., *Handbook of Treatment of Mental Disorders in Childhood and Adolescence.* Englewood Cliffs, N.J.: Prentice Hall, 1977, pp. 354-384.

----. "Children at Risk for Manic-Depressive Illness: Possible Predictors," *American Journal of Psychiatry,* 136:9 (1979): 1206-1208.

----. "Children At-Risk for Schizophrenia," *American Journal of Psychotherapy,* 34:2 (1980): 164-177.

----. "Adolescents At-Risk for Manic-Depressive Illness," in Feinstein, S. C., and Giovacchini, P. L., eds., *Adolescent Psychiatry,* vol. 7, forthcoming.

----, and Bird, H. "A Reliability Study of the Mental Health Assessment Form for School Age Children," *Journal of American Academy of Child Psychiatry,* 17:2 (1978): 338-347.

Kety, S. S. "Studies Designed to Disentangle Genetic and Environmental Variables in Schizophrenia; Some Epistemological Questions and Answers," *American Journal of Psychiatry* 133 (1975): 1134-1137.

Kety, S. S., et al. "The Types and Prevalence of Mental Illness in the Biological and Adoptive Families of Adoptive Schizophrenics," in Rosenthal, D., and Kety, S. S., eds., *The Transmission of Schizophrenia.* Oxford: Pergamon Press, 1968, pp. 345-362.

Kringlen, E. "An Epidemiological Clinical Twin Study on Schizophrenia," in Rosenthal, D., and Kety, S. S., eds., *The Transmission of Schizophrenia.* Oxford: Pergamon Press, 1968, pp. 49-63.

Kohn, M. "Social Class and Schizophrenia: A Critical Review and A Reformulation," *Schizophrenia Bulletin,* 7 (1973): 60-79.

Koppitz, E. M. *The Bender Gestalt Test for Young Children.* New York: Grune & Stratton, 1963.

Kornestsky, C., and Mirsky, A. "On Certain Psychopharmacological and Physiological Differences Between Schizophrenics and Normal Persons," *Psychopharmacologia,* (Berlin) 8 (1966): 309-318.

Kraepelin, E., *Manic-Depressive Insanity and Paranoia.* Edinburgh: Livingston, 1921.

Langfeldt, G., "Diagnosis and Prognosis of Schizophrenia, *Proceeds of the Royal Society of Medicine,* 53 (1969): 1047-1052.

Lazarus, R. S., Averill, J. R., and Opton, E. M. "The Psychology of Coping: Issues of Research and Assessment," in Coelho, G. V., Hamburg, D. A., and Adams, J. E., eds., *Coping and Adaptation.* New York: Basic Books, 1974.

Lidz, T. *The Origin and Treatment of Schizophrenic Disorders.* New York: Basic Books, 1973.

Marcus, J. "Cerebral Functioning in Offspring of Schizophrenics: A Possible Genetic Factor," *International Journal of Mental Health* 3:1 (1974): 57-73.

----, et al. "Infants At-Risk for Schizophrenia: The Jerusalem Infant Development Project," *AMA Archives of General Psychiatry,* in press.

Marcus, J., and Mednick, S. "A Longitudinal Perspective of Children At Risk for Schizophrenia," unpublished manuscript.

Marcuse, Y., and Cornblatt, B. "Proceedings of the Society for Life History Research in Psychopathology, 1979," (in press).

Matthysse, S. "The Biology of Attention," *Schizophrenia Bulletin,* 3 (1977): 370-72.

----, and Kidd, K. K. "Estimating The Genetic Contribution to Schizophrenia," *American Journal of Psychiatry,* 133 (1976): 185-191.

Mednick, S. A. "Breakdown In Individuals at High Risk for Schizophrenia: Possible Predispositional Perinatal Factors," *Mental Hygiene,* 54 (1970): 50-63.

Mednick, S., and Schulsinger, F. "Some Premorbid Characteristics Related to Breakdown in Children with Schizophrenic Mothers," in Rosenthal, D. and Kety, S. S., eds., *The Transmission of Schizophrenia.* Oxford: Pergamon Press, 1968, pp. 267-291.

----, et al. "Perinal Perinatal Conditions and Infant Development in Children with Schizophrenic

Parents," *Social Biology* 18 (Suppl.) (1971): 103-113.

Mendlewicz, J. and Rainer, J. "Adoption Study Supporting Genetic Transmission in Manic-Depressive Illness," *Nature,* 268 (1977): 327-329.

Mendlewicz, J., Rainer, J. D., and Fleiss, J. L. "A Dominant X-linked Factor in Manic Depressive Illness; Studies with Color Blindness," in Fieve, R. R., Rosenthal, A., and Brill, H., eds., *Genetic Research in Psychiatry.* Baltimore: The Johns Hopkins University Press, 1975, pp. 241-255-

McGhie, A., and Chapman, J. "Disorders of Attention and Perception in Earlier Schizophrenia," *British Journal of Medical Psychology,* 34 (1961): 103-116.

McKinnon, J. A. "Two Semantic Forms, Neuropsychological and Psychoanalytic Descriptions," *Psychoanalysis and Contemporary Thought* 2 (1979): 25-76.

McKnew, D. W., et al. "Offspring of Patients with Affective Disorders," *British Journal of Psychiatry,* 134 (1979): 148-152.

McNeil, T. F., and Kaij, L. "Obstetric Factors in The Development of Schizophrenia: Complications in the Births of Pre-schizophrenics and in Reproduction by Schizophrenic Parents," in Wynne, L. C., Cromwell, R. L., and Matthysse, S., eds., *The Nature of Schizophrenia.* New York: John Wiley, 1978, pp. 401-429.

Orvaschel, H., et al. "The Children of Psychiatrically Disturbed Parents: Differences as a Function of the Sex of the Sick Parent," *Archives of General Psychiatry* 36 (1979): 691-695.

Pearson, J. S., and Kley, I. B. "On the Application of Genetic Expectancies as Age-Specific Base Rates in the Study of Human Behavior Disorder," *Psychological Bulletin,* 54 (1957): 406-420.

Perris, C., ed. "A Study of Bipolar (Manic-Depressive) and Unipolar Recurrent Depressive Psychoses," *Acta Psychiatrica Scandinavica,* 42 (Suppl. 194) (1966): 1-189.

Petti, T. A. "Depression in Hospitalized Child Psychiatric Patients: Approaches to Measuring Depression," *American Journal of Child Psychiatry,* 17 (1978): 49-59.

Poznanski, E. "Natural Course of Childhood Depression," *Acta paedo psychiathca,* (in press).

Prentky, R. A., Watt, N. F., and Fryer, J. H. "Longitudinal Social Competence and Adult Psychiatric Symptoms at First Hospitalization," *Schizophrenia Bulletin,* 5 (1979) 306-312.

Price, J. S. "Genetic and Phylogenetic Aspects of Mood Variation," *International Journal of Mental Health,* 1 (1972): 124-144.

Reider, R., and Nicholas, P. "Offspring of Schizophrenics III: Hyperactivity and Neurological Soft Signs," *Archives of General Psychiatry,* 36 (1979): 665-674.

Ricks, D. F., and Berry, J. C. "Family and Symptom Patterns that Precede Schizophrenia," in Roff, M., and Ricks, D. F., eds., *Life History in Psychopathology.* Minneapolis: University of Minnesota Press, 1970. pp. 31-51

Rosanoff, A. J., Handy, L. M., and Plesset, I. R. "The Etiology of Manic-Depressive Syndromes with Special Reference to Their Occurrence in Twins," *American Journal of Psychiatry,* 91 (1935): 725-726.

Rosenthal, D. "An Historical and Methodological Review of Genetic Studies of Schizophrenia," in Romano, J., ed., *The Origins of Schizophrenia.* Proceedings of the First Rochester International Conference on Schizophrenia, Rochester, N.Y. 1967, pp. 15-26.

----. *Genetic Theory and Abnormal Behavior.* New York: McGraw-Hill, 1970.

----. "The Spectrum Concept in Schizophrenic and Manic-Depressive Disorders," in Friedman, D. X., ed., *Biology of the Major Psychoses.* New York: Raven Press, 1975, pp. 19-25.

Russell, E. W., Neuringer, C., and Goldstein, G. *Assessment of Brain Damage.* New York: Wiley-Interscience, 1970.

Rutschmann, J., Cornblatt, B., and Erlenmeyer-Kimling, L. "Sustained Attention in Children At-Risk for Schizophrenia," *Archives of General Psychiatry,* 34 (1977): 571-575.

Slater, E., and Cowie, V. *The Genetics of Mental Disorders.* London: Oxford University Press, 1971.

Sobel, D. E. “Children of Schizophrenic Parents: Preliminary Observations on Early Development,” *American Journal of Psychiatry* 118 (1961): 512-519.

Spitzer, R. L., Endicott, J., and Gibbon, M. “Crossing the Border into Borderline Personality and Borderline Schizophrenia. The Development of Criteria,” *Archives of General Psychiatry* 36 (1979): 17-24.

Spring, B., and Zubin, J. “Vulnerability to Schizophrenic Episodes and Their Prevention in Adults,” in Albee, G. W., and Joffe, J. W., eds., *Primary Prevention in Psychopathology,* Hanover, N.H.: University Press of New England, 1977, pp. 254-284.

Stone, M. H. “Mania—A Guide for the Perplexed,” *Psychotherapy and Social Science Review,* 5(10) (1971): 14-18.

Stone, M. H. “Etiological Factors in Schizophrenia: A Reevaluation in the Light of Contemporary Research,” *Psychiatric Quarterly,* 50:2 (1978): 83-119.

Strauss, J., et al. “Premorbid Adjustment in Schizophrenia: Concepts, Measures, and Implications,” *Schizophrenia Bulletin,* 3:2 (1977): 182-258.

Venables, P. H. “The Electrodermal Psychophysiology of Schizophrenics and Children at Risk for Schizophrenia: Controversies and Developments,” *Schizophrenia Bulletin* 3 (1977): 28-48.

Waring, N., and Ricks, D. F. “Family Patterns of Children who Become Adult Schizophrenics,” *Journal of Nervous and Mental Disease,* 140 (1965): 351-364.

Watt, N. F. “Patterns of Childhood Social Development in Adult Schizophrenics,” *Archives of General Psychiatry,* 35 (1972): 160-165.

----. “Longitudinal Changes in the Social Behavior of Children Hospitalized for Schizophrenia as Adults,” *Journal of Nervous and Mental Disease,* 155 (1972): 42-54.

Weinberg, W. A., and Brumback, R. A. “Mania in Childhood: Case Studies and Literature Review,” *American Journal of Disease of Children,* 130 (1976): 380-385.

Weinberg, W. A., et al. "Depression in Children Referred to an Educational Diagnostic Center: Diagnosis and Treatment," *Journal of Pediatrics,* 83 (1973): 1065-72.

Welner, Z., et al. "Psychopathology in Children of Inpatients with Depression: A Controlled Study" *Journal of Nervous and Mental Disease,* 164:6 (1977): 408-413.

Wender, P. H., et al. "Crossfostering: A Research Strategy for Clarifying the Role of Genetic and Experiential Factors in the Etiology of Schizophrenia," *Archives of General Psychiatry,* 30 (1974): 121-129.

Winokur, G., Clayton, P. J., and Reich, T. *Manic Depressive Illness.* St. Louis: C. V. Mosby, 1969.

Wynne, L. C., and Singer, M. T. "Principles for Scoring Communication Defects and Deviances of Parents of Schizophrenics in Psychological Test Transactions," *NIMH Annual Report,* M.H. Intramural Research Programs, 1972, pp. 11-13.

Youngerman, J., and Canino, I. "Lithium Carbonate Use in Children and Adolescents," *Archives of General Psychiatry,* 35 (1978): 216-224. no. Zerbin-Rudin, E. "Schizophrenic Head Injured Persons and Their Families," Abstract 356, Report of 3rd International Congress on Human Genetics, Chicago, 1966.

----. "The Genetics of Schizophrenia: An International Survey," *Psychiatric Quarterly,* 46 (1972): 371-383.

Zubin, J., and Spring, B. "Vulnerability—A New View of Schizophrenia," *Journal of Abnormal Psychology,* 86:2 (1977): 103-126.

Notes

1 The need for careful diagnosis in order to distinguish a schizophrenic genotype from a similar phenocopy is demonstrated by the genetic studies. There are many imitations of schizophrenia, such as temporal lobe epilepsy and manic psychosis (both can resemble an acute schizophrenic reaction). Careful family and developmental history are often helpful in resolving the problem.

2 Pregnancy Complications = PC; Birth Complications = BC; Neonatal Complications = NC; Obstetrical

Complications = OC.

3 The CPT, a measure of sustained attention, involves a succession of playing cards projected onto a screen. The subject's task is to respond when two identical slides appear in sequence, such as the six of clubs followed by the six of clubs. Half the trials are presented without distraction and half are presented in the presence of external auditory distraction (a tape recorded female voice reciting numbers at varying speeds and tones). A false response is considered incorrect (when the subject responds to a six of clubs, for example, followed by a six of hearts).

4 This case is not connected with any of the high-risk projects under discussion.

5 Odd communication without formal thought disorder, self-referential thinking, suspiciousness, depersonalization, magical thinking, inadequate rapport, hypersensitivity, and social isolation.