conference on possible followup of NINCDS collaborative perinatal study*

Bette Runck

Records from a massive 20-year NIH study of neurological disorders in children could shed light on the childhood antecedents of adult psychopathology.

But a group of scientists who met at NIMH recently agreed that although the study's data base may be unique in science—it covers 40,000 children from before birth to age 7—it has limited usefulness for research on mental illness.

The NINCDS Collaborative Perinatal Project (NCPP) on the perinatal origins of childhood neurological disorders has been done through the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS). It attempted to verify findings of previous retrospective evaluations that had shown that children with mental retardation, cerebral palsy, and birth defects had more often suffered perinatal insults than had normal children.

When the project was started, the difficulties of doing such large-scale collaborative research were less obvious than they are today, partly because of the experience gained by the NINCDS scientists during the course of the project.

Between 1959 and 1965, 55,908 pregnant women registered with the 14 university-affiliated medical centers that collaborated in the project. The women were regularly checked throughout pregnancy and monitored during labor and delivery. Their infants were given physical and neurological examinations.

The children, who were further examined at intervals until they were 7, were given psychological tests at 8 months, 4 years, and 7 years. Speech and hearing were evaluated in half of the children at age 8.

During the next 5 years, all the children will reach the age when adult schizophrenia begins to appear. Of the 40,000 on whom there are complete records, about 400 will in time become schizophrenic.

Tantalized by these records, the NIMH Center for Studies of Schizophrenia invited NINCDS researchers and others who have used the NCPP data base to describe their research at a 1-day conference last April.¹ Together with NIMH scientists and others doing research on schizophrenia, the NINCDS investigators explored the possibility of following the children further to learn which of them develop schizophrenia or other mental disorders. The readily available early developmental histories of the mentally ill subjects could then be compared to those of the normal subjects.

Among the studies that have already used the NCPP data, several focused on mental illness or conditions associated with psychosocial disturbances. One, reported by Dr. Sarah H. Broman of the NINCDS Developmental Neurology Branch, examined the antecedents of learning disorders and mental retardation. She said that cognitive deficits and behavioral deviations in the preschool period and socioenvironmental factors were associated with low achievement in children with normal IQ's.

NINCDS scientist Dr. Karin B. Nelson earlier reported findings on cerebral palsy and seizure disorders.

One study of early childhood psychosis among the NCPP sample was described by Dr. E. Fuller Torrey, who is now with St. Elizabeths Hospital, Washington, D.C. Torrey, who also organized and chaired the conference, said that among 26 perinatal factors examined in the records of 14 autistic children, only one appeared to be associated with the disorder. Two-thirds of the

*Reprint requests should be addressed to the author at NIMH, Rm. 15C-17, 5600 Fishers Lane, Rockville, Md. 20857.

¹A list of participants is provided at the end of this report.
mothers of the autistic children had experienced uterine bleeding during pregnancy, especially during the second trimester. Further analysis of the records of six additional psychotic children in the sample showed that proportionately more of their mothers, too, suffered bleeding in pregnancy (Torrey, Hersh, and McCabe 1975).

The scientists who attended the conference had been drawn by the possibility of doing more of this type of research. Such prospective studies are highly prized because they circumvent the errors of retrospective analyses—the temptation for both subjects and researchers to reconstruct the past to fit preconceived ideas. Discussion of the NCPP demonstrated, however, that prospective studies are fraught with their own difficulties.

Several investigators, reporting on studies that have used the NCPP data, noted that there was variation among the 14 centers. For example, the rate of followup of the subjects at age 7 varied from 65 percent at some centers to more than 95 percent at others.

Even without these difficulties with the existing data base, followup of the entire sample would be prohibitively expensive to undertake—especially since the yield from such research is not likely to be great. In studying schizophrenia, for example, half a century will pass before the NCPP children live through the lifetime risk period. Even if followup of the entire sample were begun now, many of the 400 who are expected to develop schizophrenia will have been lost to study. Sample sizes would be too small to produce meaningful results. A shorter term followup would identify only early-onset cases, and sample sizes would be still smaller. The conference participants agreed that, rather than focus only on schizophrenia, it would be more fruitful to examine a whole range of psychopathology—including, for example, manic-depressive psychosis, alcoholism, and sociopathy.

Alternative strategies for following some part of the total sample were suggested. One would focus on factors that have been hypothesized to be linked to mental disorder. A second would involve routine administration of simple tests of psychopathology to portions of the sample that are already being followed. A third would focus on the children of parents with a known history of mental disorder.

Dr. Ronald O. Rieder, research psychiatrist in the NIMH Laboratory of Psychology, recommended the first strategy—selecting a sample of children with known perinatal difficulties. Among the factors that Rieder said might be etiologically significant are vaginal bleeding, edema, and hypertension during pregnancy, the use of anesthesia during delivery, and hyperbilirubinemia, seizures, or hypoglycemia in infancy. Such a design would show if these early conditions have lasting consequences for the child’s mental health.

The second strategy—using samples that are already being followed beyond the age of 8—was suggested by Dr. Loren R. Mosher, Chief of the NIMH Center for Studies of Schizophrenia. Mosher said that the Philadelphia sample, which accounts for more than a fifth of the total NCPP data base, was a likely choice for such a study since followup was already underway. Easily administered tests of psychopathology could be added without much expense. The Philadelphia investigators, who had described their efforts to determine childhood precursors of obesity, hypertension, and other conditions, noted that they can now locate about 90 percent of the children who completed the 7-year study, but that one in nine of these refuses to come in for further testing. Cost of this followup, they said, was about $85 per case. They also pointed out that this sample was drawn exclusively from the maternity ward of the Pennsylvania Hospital; 99 percent of all mothers on this ward participated in the Philadelphia portion of the NCPP.

A third research design discussed at the conference—studying only the children of psychiatrically disturbed parents—has already been used in two investigations of children with a schizophrenic parent in the NINCDS project.

Using the Boston sample, Rieder found an unusually high rate of perinatal deaths in the offspring of schizophrenic women. His research also showed a relationship between IQ and perinatal complications in the children of schizophrenics—a relationship that was absent in normal subjects (Rieder et al. 1975 and Rieder, Broman, and Rosenthal 1977).

University of Minnesota psychologist Dr. Irving I. Gottesman reported on another study of the NINCDS children with schizophrenic parents, this one using the Minnesota sample. He and his colleagues D.R. Hanson and L.L. Heston found that the children of schizophrenics were “remarkably normal on a host of pregnancy and delivery variables, neurological examinations, physical growth measures, and psychological tests” (Hanson, Gottesman, and Heston 1976, p. 142). Gottes-
man's group did find, however, that five of the children of schizophrenics (17 percent) "have an enduring pattern of maladjustment, and have exhibited behaviours often reported in the premorbid development of schizophrenia" (p. 150). None of the controls showed such a pattern. The Minnesota group concluded that while this study is only exploratory, it does suggest specific variables of theoretical and clinical interest.

A third study of the children of mentally ill parents in the NINCDS sample, which has just gotten underway at the New York State Psychiatric Institute, was described by Dr. Yvonne Stellingwerf and Dr. L. Erlenmeyer-Kimling.

The Boston, Minnesota, and New York studies all focused on the offspring of mentally ill parents because evidence has shown that these children are at greater risk for future breakdown. All three studies relied upon existing NCPP data and the parents' psychiatric records.

Rieder mentioned that ethical issues are involved in doing further research on these children. He pointed out that the mothers originally agreed to be in a study of mental retardation, cerebral palsy, and other neurological disorders. To identify the high risk children and ask them to participate in future studies may be an invasion of privacy, Rieder said. It may also have an adverse effect on them and their families.

Another objection to such studies was raised by Mosher, who noted that NIMH is already supporting a number of sophisticated prospective studies using the high risk approach.

Despite the reservations about doing long-term high risk studies or focusing only on schizophrenia, the conference participants felt it might well be possible to use the unique NCPP sample to study mental disorders. They also appeared to have gained insights from the discussion into the difficulties encountered in large-scale prospective studies.

A bibliography of publications that have grown out of the NCPP is available from Dr. Joseph S. Drage, Chief, Developmental Neurology Branch, Federal Building, Room 816, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Md. 20014.

References


Conference Participants

Outside Consultants

Dr. Richard W. Brunstetter
Tulane University School of Medicine
New Orleans, La.

Dr. C. Hal Brunt
University of Tennessee at Memphis
Memphis, Tenn.

Dr. Robert Cancro
New York University Medical Center
New York, N.Y.

Dr. William T. Carpenter, Jr.
Maryland Psychiatric Research Center
Baltimore, Md.

Dr. L. Erlenmeyer-Kimling
New York State Psychiatric Institute
New York, N.Y.

Dr. Edward F. Foulks
Hospital of the University of Pennsylvania

Dr. Rachel Gittelman-Klein
Long Island Jewish Hillside Medical Center
Glen Oaks, N.Y.

Dr. Irving I. Gottesman
University of Minnesota
Minneapolis, Minn.
schizophrenia—is there an answer?

What is schizophrenia? What causes it? How is it treated? What is the outlook for its control? These are the questions addressed in a booklet prepared by the NIMH Center for Studies of Schizophrenia.

Directed to readers who have little or no professional training in schizophrenia-related disciplines, the booklet gives qualified explanations of some of the complex issues concerning schizophrenia. It also conveys something of the despair, sense of unreality, fear, and loneliness that a schizophrenic individual experiences.

The booklet describes "The World of the Schizophrenic" through the use of analogy and the words of patients. It briefly tells what is known about causes—the influence of genetics, family, environment, and biochemistry. It discusses common treatment techniques. The booklet closes with a discussion of the prospects for understanding schizophrenia in the coming decade and the outlook for individuals who are now victims of this most prevalent mental disorder.

Single copies of Schizophrenia—Is There an Answer? (DHEW Publication No. ADM 74-24) are available from Public Inquiries, National Institute of Mental Health, Room 505, 11400 Rockville Pike, Rockville, Md. 20852.