In 1972 a seven-man delegation from the National Institute of Mental Health visited the Soviet Union to discuss brain research on schizophrenia with Soviet colleagues. The trip was the outcome of several years of informal contacts between researchers in both countries which, in November 1971, culminated in a specific invitation from Professor A. V. Snezhnevsky, Director of the Institute of Psychiatry in Moscow, to Dr. Bertram S. Brown, Director of NIMH. Dr. Brown was accompanied on the trip by Dr. Irwin J. Kopin, Chief of the Laboratory of Clinical Science; Dr. Morton Kramer, Chief of the Biometry Branch; Dr. Loren R. Mosher, Chief of the Center for Studies of Schizophrenia; Dr. William N. Pollin, Chief of the Twin and Sibling Studies Branch; Dr. Gian C. Salmoiraghi, Director of the Division of Special Mental Health Research; and Dr. E. Fuller Torrey, Special Assistant to the Director for International Activities.

Prior to the visit our knowledge of Soviet research was restricted to presentations at international meetings and to the few Soviet publications which had been translated into English. In both cases there is a tradition in Soviet research of presenting research results in summary form with less detail on methodology than we are accustomed to. Knowledge of Soviet research in the United States was sharply limited to the few researchers who had visited the U.S.S.R. and/or could read sufficient Russian to keep up with developments in Soviet scientific journals. Compared with Western European countries, we knew little about ongoing research in the Soviet Union. By contrast Soviet researchers read American journals and are very well acquainted with our research. For these reasons, it seemed important to make a visit of sufficient duration to allow time to sit down with our Soviet colleagues in their laboratories and discuss specific methodologies and research directions.

The organization of medical research in the U.S.S.R. differs from its organization in this country. For example, the Institute of Psychiatry in Moscow is under the Soviet Academy of Medical Sciences and, as such, reports on all schizophrenia research directly to the
The Academy in turn gets its budget from the national Ministry of Health but has relative autonomy to set its own goals and priorities. The Academy designates different institutions to lead research efforts on specific problems, and the Institute of Psychiatry had been designated to lead research on schizophrenia. The idea is not dissimilar to the "lead agency" concept which has become increasingly utilized in the Federal U.S. Government in recent years.

This does not mean that other institutions in the U.S.S.R. do not do research on schizophrenia, of course, but only that the Institute of Psychiatry in Moscow is the lead institution and, with the Academy of Medical Sciences, tries to coordinate and integrate research efforts on the disease. All 15 Republics which constitute the U.S.S.R. have institutes and/or departments of psychiatry which may also do some research in this field. Other institutes of the Russian Republic (in which Moscow is located) and those in the Georgian Republic are known to be especially active in schizophrenia research. These institutions are directly under the Ministry of Health for their respective Republics and are not directly associated with the Academy of Medical Sciences.

The organization of research in the U.S.S.R. raises many important questions when one compares it to our own organization. Having a lead research institute on a specific problem has the attractiveness of theoretically minimizing overlap, though whether this happens in fact could not be ascertained from our observations. Such coordination would be effective only insofar as open and frequent communication exists between the different research institutions. In the Soviet Union the vast distances appear to make such communication less than optimal. Another precondition for the effectiveness of such a system would be a relative ease of mobility of researchers from one research institute to another so that, for instance, when a schizophrenia researcher accidentally finds some data which opens up a potentially productive area of research on epilepsy, he can then negotiate to transfer to the research institution where such research is taking place.

The lead institute idea did appear to produce an impressive degree of integrated research efforts on schizophrenia within the Institute of Psychiatry. The Institute was divided into six basic divisions and the flow of expertise and information among them was impressive. The Department of Clinical Studies charts the clinical course of schizophrenia patients in different age groups and is working toward a systematization of the main forms of the disease. The Department of Epidemiology studies the incidence and prevalence of schizophrenia within the population. The Laboratory of Pathopsychology studies the structure of cognitive processes (thinking, speech, perception) in patients with schizophrenia. The Laboratory of Neurophysiology studies the bioelectrical activity in the brains of schizophrenic patients and also in their relatives. The Laboratory of Pathophysiology studies the biochemistry, immunological reactions, blood cells, and genetic characteristics of the patients. Finally, the Laboratory of Experimental Pathology and Brain Pathomorphology studies anatomical and cytochemical changes in the brain and blood tissues.

One problem raised by the lead institute concept is the support of basic research. If research is goal directed and targeted toward specific problem areas, as in the U.S.S.R., does this mean that basic research receives less support? In all areas of research it is necessary to have work going on at the basic level; for instance the eventual unraveling of schizophrenia may not take place until there is a better understanding of the biochemistry of brain cells, and this biochemical research is not disease specific but rather basic to all brain diseases. In the United States we have not yet solved the problem of how to measure basic against applied research, and our observations in the U.S.S.R. indicated that the problem had not been solved there either. Getting the most for each research dollar spent demands that we continue to work toward the most optimal mix of these two types of research.

Another characteristic of Soviet schizophrenia research is that it is clinically centered. Virtually all the research psychiatrists at the Institute of Psychiatry retained some clinical responsibilities in the adjoining Kashchenko Mental Hospital and spent part of each week seeing patients. The Director of the Institute of Psychiatry, Professor A. V. Snezhnevsky, is highly...
regarded as a clinician. This continuing emphasis on clinical work as the basis for good research is seen even in the work of the Minister of Health in the U.S.S.R., Dr. Boris V. Petrovsky, who does surgery every week in addition to his administrative responsibilities.

The NIMH delegation was also favorably impressed by the potential for followup studies of schizophrenic patients in the U.S.S.R. Patients are closely followed in outpatient clinics once they leave the hospital and their course can be carefully and accurately charted. The records available on the long-term course are frequently more complete and accurate than those available in this country where less coordination between inpatient and outpatient facilities takes place.

An understanding of schizophrenia research in the U.S.S.R. necessitates an understanding of the system of classification of the disease used there. This system is based upon the clinical work of Professor Snezhnevsky and his colleagues and differs from the classification used in the United States. Before any real research collaboration can occur between the two countries in schizophrenia research, it will be necessary to try to find a common denominator for the two classificatory systems. An American geneticist must know what is meant by a Soviet claim of the occurrence of schizophrenia in "shift-like" forms of the disease and a Soviet researcher must be able to understand the same claim for the "chronic hebephrenic" form of the disease. The NIMH mission began a dialogue on this and has undertaken concrete steps to work toward a common denominator.

In a oversimplified form, Soviet clinicians classify schizophrenic patients more on the basis of the long-term clinical course and less on the basis of the acute symptoms seen in a patient at any given time. Thus the three main divisions are the continuous form with slow but progressive deterioration; the shift-like form with acute episodes but residual symptoms (mild to moderate personality change) between attacks; and the periodical form with acute attacks but no residual symptoms between attacks. All three main forms have many subcategories.

From discussions at the Institute of Psychiatry, as well as trips to Leningrad, Kiev, and Tbilisi to visit the major psychiatric research facilities in those cities, members of the NIMH delegation obtained an overview of Soviet research on schizophrenia in many areas. In a brief summary like this, it is not possible to describe all areas explored. Rather a few areas will be selected for discussion to give some idea of the range and major thrusts in the U.S.S.R. compared with what is going on in the United States in this field. It may be seen that an exchange of information between researchers could be useful for both countries.

Biochemical Aspects

The pursuit of a biological basis for the development of one of the several clinical forms of schizophrenia identified by the Russian clinicians has been largely directed at attempts to demonstrate an abnormal, toxic factor in the serum of schizophrenic subjects. The methods used to identify the presence of such a plasma factor have varied with the investigator and with time, but the basic premise has remained unchanged.

The techniques used include studies of the effect of serum of schizophrenic patients (or a partially purified derivative) on 1) the activity of neurones (spontaneous activity of neurones in the esophageal ganglion of a snail); 2) the electron microscopic structure of lymphocytes in culture; 3) the membrane permeability of red blood cells to LDH and the effects of such changes in permeability on lactate/pyruvate ratios; 4) the demonstration by complement fixation of antibrain antibodies and definition of the characteristics of such antibodies; and 5) alterations of the myelination of rat embryonal gasserian nodes in culture.

Other studies have been directed towards understanding the metabolism of drugs (e.g., chlorpromazine) used in the treatment of schizophrenia and effects of antipsychotic agents (e.g., lithium) on mitochondrial metabolism (ATP).

Results of some of the studies are provocative, but difficulties in replication have been encountered. Similar studies are in progress in some laboratories in the United States and communication would be valuable to establish more uniform techniques for examination of the serum for abnormal factors. It would also be of interest to attempt to reconcile the protein factor hypothesis with the "amine" hypothesis which is more popular in our country and in Western Europe. The cooperation of two groups of investigators using similar criteria for diagnosis of schizophrenia and similar laboratory methods for identification, separation and testing of serum components would be valuable.
Genetic Aspects

Genetic research in the U.S.S.R. must be seen against the background of the controversies and consequences that surrounded the theories of Lysenko some decades ago. In essence a whole generation of geneticists and genetic research is missing on the Soviet scene. This leads to obvious problems and simultaneously a new high level of interest and support.

The genetics of schizophrenia appears to be an area of particular interest at the Institute of Psychiatry in Moscow. Soviet psychiatry has difficulty in dealing with the possible role of social factors, such as socioeconomic class, in pathogenesis because of views concerning the results of social engineering. There is also skepticism about interpersonal and intrafamilial determinants; such approaches apparently are seen as being contaminated by Freudian dogma. If one thus eliminates or downplays both social and familial factors, there is then a necessarily increased emphasis that must be placed upon genetic explanations.

Three types of work go on at the present time in the Institute that are relevant to genetic studies in schizophrenia. One is a classical type of clinical genetic study. The clinical genetic group has interviewed all relatives of a large consecutive \( N > 300 \) series of schizophrenia admissions. The basic design of this type of study is to evaluate the personality and diagnosable psychopathology in different categories of relatives, then to explore the relationship between patient's and relative's diagnoses, and determine to what extent, if any, these are consistent with various genetic formulations. There are methodological problems with this work, and though the results warrant our attention and analysis, they do not appear to offer any especially new promise.

A second approach focuses upon biological rather than clinical psychiatric evaluations of the relatives of schizophrenic patients. Many of the techniques which the Russians have developed in an effort to study various biological parameters of schizophrenia (antibody titers, LDH, immunologic measures, etc.) have been used with family members as well as with index cases of schizophrenia. A third type of work initiated by Dr. Victor Gindilis attempts to test empirically certain theoretical approaches previously propounded by Darlington, Slater, and others. These suggest that even in monozygotic twins there are significant genetic organic differences because of chromosomal/cytoplasmic asymmetry or the interaction of one gene upon others. Dr. Gindilis is attempting to evaluate such theories, and their possible relationship to the pathogenesis of schizophrenia, by sophisticated efforts to compare the degree to which MZ twins concordant for schizophrenia are similar with respect to different biological variables. He hopes thereby to identify which of these variables are intrinsically related to the pathogenesis of schizophrenia.

In all of these studies considerable emphasis is placed upon the Institute's system of diagnosis, and its categorization of schizophrenia. There are numerous reports of finding significant genetic as well as biological differences among their three major categories of schizophrenia. More intensive analyses of these findings seem desirable.

Epidemiological Aspects

Our Soviet colleagues attach much significance to epidemiological research on schizophrenia in their search for causes of this disorder. Professor Snezhnevsky (1968, p. 443) has emphasized that in research on schizophrenia "one should employ clinical, pathophysiological, social, epidemiological and all forms of available biological methods." Lozovsky (1968, p. 200) has stated: "It may also be assumed a more or less full understanding of the nature and essence of schizophrenia cannot be obtained only with the aid of biological methods; it requires a comprehensive study including pathopsychological, clinical and sociological investigations."

The Head of the Epidemiological Department of the Institute of Psychiatry of the Academy of Medical Sciences is Dr. Anatoley B. Smulevich. This Department has the following sections:

1) An epidemiological section which concentrates on studies of the frequency of occurrence of schizophrenia in various population groups.

2) A clinical section which carries out a series of studies on the regularities in the development of schizophrenia. Illustrative of the areas of concern of the research workers in this group are a clinic-epidemiological study of favorably developing forms and remissions in schizophrenia; types of remissions and regularities in their development; psychopathology of favorably developing forms and remissions; the treatment of schizophrenia; and social readaptation of
schizophrenic patients in industry, sheltered workshops, in rural areas.

3) A section for the coordination and planning of research. This group serves as a Field Research Center in relation to WHO activities. This includes the International Study of Manic States and the WHO program of Standardization of Diagnosis Classification and Statistics of Mental Disorders.

Dr. Smulevich emphasized what he believes to be unique opportunities for epidemiologic research on schizophrenia afforded by the Institute's research program and the Soviet system for patient care for the mentally ill. First, the psychiatrists trained at the Institute use uniform diagnostic criteria for schizophrenia. A glossary of standard definitions of the syndromes in schizophrenia makes it possible to identify practically all schizophrenic states and to code them for statistical purposes. Second, the Soviet system of medical care for the mentally ill provides for special registration of all cases of mental disorders seen by a psychiatrist either in a mental hospital or dispensary. Also, every patient is personally examined by a clinician, and finally, the official population censuses of 1959 and 1970 provide basic data on the demographic characteristics of the population.

Dr. Smulevich made available to the delegation a series of tables he and his staff have developed on distributions of various features of "attack-like" schizophrenia by age of onset, sex, and frequency of attacks. He also described clinical epidemiological studies of remissions in schizophrenia, with special reference to the social adaptation of the patient. This concept takes into account both the patient's ability to work and his clinical state and is reflected in the following classification of degrees of work disability: 1) patient cannot take care of himself, 2) patient is able to work in industry and to take care of himself at home, 3) patient's ability to work is limited. These studies are being carried out in three districts of Moscow, each with a population of 200,000 to 300,000 persons. Dr. Smulevich estimated that there are about 1,250 schizophrenics in each of these districts, a prevalence of 4 to 6 per 1,000. Dr. Smulevich also states that about two-thirds of schizophrenics, regardless of type, can live at home and most are ambulatory.

The epidemiological group has also developed an extensive schedule for use in their various studies. This schedule provides information on demographic characteristics of the patient, diagnosis, history of illness, current clinical status, hereditary factors, patient's pre-morbid characteristics and his childhood background. It provides additional information on the social situation of the patient at time of examination, important features in the dynamics of illness, indices of social and occupational adaptation, and the sources of information.

The Institute, then, is carrying out an extensive and intensive epidemiologic research program on schizophrenia. At this point it is difficult to make comparisons between findings in their studies and those done in the United States because of the differences in case-finding methods, diagnostic and assessment procedures, and the organization of their psychiatric service. The development of a collaborative research program might overcome these difficulties by developing clinical, followup and data collection procedures that could be applied in a standardized and uniform fashion in the United States and the U.S.S.R. Such research would make it possible to determine the extent to which differences may exist in rates of occurrence of schizophrenia in Soviet and American communities and in the course and outcome of illness in the patients that would be studied.

**Microbiological Aspects**

Microbiological aspects of schizophrenia have a long history in the U.S.S.R. During the early part of the century it was believed that bacterial infection might play a role in the disease. These were eventually discarded and replaced by theories of viral infection. In the 1950's extensive examination of the serum and spinal fluid of schizophrenic patients in the U.S.S.R. showed elevated viral antibody levels as measured by the tests then available. Subsequent research claimed to have located virus-like corpuscles in the spinal fluid of almost half of the schizophrenics. This work has not been followed up in the U.S.S.R., but is of interest in view of the new models of slow and latent virus diseases recently found in the United States. As attention is turned toward viruses and their possible relationship to schizophrenia, it is important to review the earlier Soviet work...
and maintain contact with Soviet researchers who are still interested in it.

The outcome of the NIMH mission was a "Memorandum of Understanding" which was signed by both Professor Snezhnevsky and Dr. Brown. The memorandum stated an intention to submit plans for collaborative research on schizophrenia to the U.S.-U.S.S.R. Joint Committee for Health Cooperation at its next meeting. The plans outline possibilities for standardizing the categorization of main forms of schizophrenia and specific collaborative research projects in such areas as the biochemical, genetic, immunological, neurophysiological, microbiological, and epidemiological aspects of the disease. At its meeting in Washington in March 1973 the U.S.-U.S.S.R. Joint Committee accepted these plans as part of the health agreement between the two countries. Implementation of the plan is now underway.

References


an invitation to readers

Providing a forum for a lively exchange of ideas ranks high among the Schizophrenia Bulletin’s objectives. In the section, At Issue, readers are asked to comment on specific controversial subjects that merit wide discussion. But remarks need not be confined to the issues we have identified. At Issue is open to any schizophrenia-related topic that needs airing. It is a place for readers to discuss articles that appear in the Bulletin or elsewhere in the professional literature, to report informally on experiences in the clinic, laboratory, or community, and to share ideas—including those that might seem to be radical notions. We welcome all comments.—The Editors.

Send your remarks to: At Issue
Center for Studies of Schizophrenia
National Institute of Mental Health
5600 Fishers Lane
Rockville, Md. 20852