ethical and legal considerations in high risk studies of schizophrenia

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The domains of the legal and mental health systems have long been interrelated; today their joint concerns seem focused on the broad issues of ethics and morals. Over the past several years, there has been a crescendoing involvement of the legal system in mental health issues; informed consent, confidentiality, right to treatment, and legal rights of patients have been brought into sharp relief by court cases and/or new regulations.

No area in which these two domains overlap is more perplexing than one involving children. For example, what are the legal rights and responsibilities of children? When are children able to make decisions in their own behalf? If they are deemed unable to decide for themselves, who should? How are they to be protected from being subjected to possibly harmful procedures, and at the same time assured that they will not be denied new treatments of potential value? Although this is only a partial listing of troubling ethical quandaries regarding the treatment of children, it can easily be seen that similar questions can be raised with regard to adults as well. Professor Curran's summary of an intensive review of the legal, ethical, and moral implications of intervention undertaken with children thought to be vulnerable to psychopathology in later life is presented here, in part, to serve as a stimulus for Bulletin readers to air their views, experiences, and problems with the entire spectrum of legal, ethical, and moral issues that confront mental health workers today. We invite your comments and will publish a representative sampling of material received. Preference will be given to letters that provide data documenting views, experiences, and problems.—The Editors.

In recent years, the National Institute of Mental Health has given high priority to the encouragement and support of etiological investigations of schizophrenia. Among the projects in this area that have the most potential for producing significant findings are the longitudinal studies of children believed to be at high risk for the disorder. During 1972 and 1973, the NIMH was supporting 11 studies of this type, 9 in the United States, 1 in Denmark, and 1 in Sweden. Because of the present concern in this country about legal and ethical matters in medical investigation, the NIMH Center for Studies of Schizophrenia supported a project, on which I was principal investigator, to review the issues involved in long-term psychiatric research, with particular attention to intervention with children at high risk for schizophrenia. This review was begun in the summer of 1972 and was concluded on July 1, 1973.

To carry out the review, I site-visited the majority of ongoing high risk studies in the United States, and I also participated in a 3-day conference attended by nearly all participants. The 254-page final report (Curran 1973) on the project was submitted to the Center for Studies of Schizophrenia on July 1, 1973. Appendices were added which provide an annotated bibliography of the legal, ethical, and scientific literature in the field and special legal studies of consent of minors to medical treatment, rights of minors and their parents, school law on research studies of pupils, legal impediments of the mentally ill in marriage, divorce, and sterilization, and legal regulation of confidentiality and privacy in psychiatric research in those States where high risk studies are now being conducted.
high risk investigators in Puerto Rico in October 1972. Excellent cooperation was received throughout the study from all of the projects, and investigators talked frankly about their own ethical and legal concerns in the projects and in psychiatric research generally. Documentation relating to subject consent forms used and clearances obtained from institutional review committees was received from most of the projects. Although confidential research files and subject records were not examined, either I or my associates reviewed in detail all papers published by the investigators concerning their high risk studies.

**General Trends in Regulation**

At the outset, it is important to place this study in perspective in relation to the general atmosphere of regulation of human investigation in the United States in these early years of the 1970's. There can be no doubt but that the present political trend is toward increased legal regulation and control. The Nation is moving away from the informal standards of professional ethics developed in medicine and science over the centuries and toward a civilly enforced body of law and administrative agency regulations and guidelines that will control research projects and the use of humans in such projects. Furthermore, the regulatory program being developed is national in character and direction, not State or local. It is essentially centralized and monolithic, with principles of regulation being applied across the board to all types of medical and scientific research involving humans, with little or no distinction between fields. An earlier paper (Curran 1961) described in detail the evolution of this regulatory program in the Federal Government.

Because of its national character, the developing regulatory system is highly subject to periodic restructuring and reorganization, which may be quite drastic in form and substance as a result of changing views in Congress, in the Presidency, and in the Federal agencies themselves. Publicity concerning ethical abuses in individual research projects may result in strident outcries to punish the abusers and to install restrictive measures against similar incidents. Quite recently such a response occurred in the aftermath of the so-called Tuskegee Syphilis Study (U.S. Department of Health, Education, and Welfare 1973b). The official report on the study recommended a substantial revision of the Federal regulatory program and the establishment of a powerful national commission to control not only federally supported research projects, but all research on humans in the United States. Senator Edward M. Kennedy submitted to the 1974 session of Congress a bill (H.R. 7724) incorporating these recommendations and proposing the establishment of a National Commission for the Protection of Human Subjects of Biomedical Research. The U.S. Department of Health, Education, and Welfare (1973a and 1973c) also held its own review of the area and issued new proposed regulations that would reorganize the institutional review system and provide much more stringent standards for the use of different types of research subjects and patients.

Note should also be taken of other broad trends in American society that have an important effect upon this subject. Most significant is the civil rights movement in our political life and in our courts. The movement can be marked essentially from the Civil War and the adoption of the Thirteenth and Fourteenth Amendments to the Constitution in the 1860's, but it received its primary emphasis with the so-called "Warren Court" and Brown v. Board of Education in 1954. Since that time, case after case has expanded the rights of individuals in a multitude of situations that culminated politically in the Civil Rights Act of 1964. Among the areas receiving special attention at present are the rights of women, children, prisoners, mental patients, alcoholics, and drug addicts.

Finally, note should be taken of the specific adoption of bills of rights for medical patients (American Hospital Association 1972), the establishment of advocacy programs to protect various medical patient groups (Annas and Healey 1974), and the growth of malpractice suits against medical personnel and hospitals (U.S. Department of Health, Education, and Welfare 1973d).

All of these factors, in a cumulative way, create a climate of great sensitivity to abuses of the rights and welfare of human subjects and patients in medical research of any kind.

**Critical Issues in High Risk Studies**

Any attempt to assess the critical issues in high risk studies in schizophrenia must take into account three key factors that characterize these studies: 1) they are psychiatric studies, 2) children are the primary subjects, and 3) most of the studies are of a long-term, prospec-
nature involving extensive observation and potential therapeutic intervention in the lives of the subjects.

Of all medical research, psychiatric studies are among the most sensitive and vulnerable to legal scrutiny. Matters of confidentiality and privacy are particularly acute, as the social stigma of mental illness is still very great in our society. Restrictions on the use of mental patients as subjects are growing steadily, both because of these patients' limited capacity to give valid consent and because of their confinement in institutions.

The fact that high risk studies involve children as their main focus also occasions special difficulties, since children are considered the most vulnerable of all research subjects and are consequently surrounded by the most restrictive barriers to their utilization.

The long-term nature of high risk studies presents ethical and legal issues of a more novel nature. Although surprisingly little attention has been given to long-term investigations in the psychiatric literature or in the laws and regulations on clinical investigation, such studies present special problems by the very circumstance of the passage of time, accumulation of information, and changing conditions both within the study and in the outside world.

Ethical Justification: Threshold Issues

The issues of ethical justification are three in number: 1) the significance of the research, 2) the relevance of the questions asked and hypotheses to be tested, and 3) the overall quality of the research design. I call these threshold issues because they are raised before research begins and before subjects are selected.

The landmark exposition of the ethical justification for medical experimentation came in the Nuremberg Code. Principles 2 and 3 follow:

The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random or unnecessary in nature. [Principle No. 2]

The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment. [Principle No. 3]

At the threshold, when research results cannot be predicted with any degree of certainty, the requirement of potential fruitfulness or significance is not a very high barrier to overcome; hence the reference to "not random or insignificant" in Principle 2. Beecher (1959) has said that the research, at the outset, should not be found trivial in nature. Sheps (1962), in a very perceptive paper, added that the research must not be unnecessarily repetitive of other accepted, competent research.

The questions asked by the researchers must not be inherently unethical, illegal, or immoral. For example, one cannot test two different types of lethal drugs merely to see which kills its victims faster or with the least evidence of violence.

The issue of the quality of the research design is essentially one of degree. A very poorly designed project, which cannot possibly yield the results sought, cannot justify exposing human beings to any form of risk or inconvenience. Also, Rutstein (1969) has asserted that a research design without controls is unethical. The only exception he would make is in a situation in which the disease being treated is 100 percent fatal.

Justification of High Risk Studies

When examined in regard to the potential medical significance of the research, these high risk schizophrenia investigations must be given high marks. Schizophrenia is one of the most prevalent and serious of the mental disorders. Until the 1960's, mentally ill persons occupied half the hospital beds in the United States, and schizophrenics accounted for more than the majority of these patients. In recent years, the number of hospital beds occupied by mental patients has declined, but it is not at all clear that the actual incidence of schizophrenia has itself decreased over this same period. The disorder has remained essentially chronic in nature and is estimated to afflict from 1 to 3 percent of the total population of the United States. In 1969, nearly 70 percent of all patients admitted with a diagnosis of schizophrenia had received hospital care previously. Despite its importance, research on the etiology of schizophrenia has never received the relative support it deserves, and much remains to be learned about the disorder. As late as 1971, Mosher and Feinsilver reported:

To this day, profound disagreement exists as to what properly constitutes schizophrenia and how—and whether—this complex disorder should be classified. [p. 2]
On the questions posed and the research designs used, the high risk studies again score well. Previous etiological studies of schizophrenia have nearly all been retrospective and thus subject to the well-known weaknesses of such investigations. With a disease prevalence of only 1 to 3 percent, a general population sample is not particularly feasible for prospective studies because the sample would have to be very large to produce many positive cases. Longitudinal researchers have therefore sought various methods of finding smaller samples that can be expected to yield much higher ratios of schizophrenic patients in later life (Garmezy, in preparation). The most productive of the high risk groups as yet discovered are the offspring of schizophrenic parents. Epidemiological studies have established rates of schizophrenia that range between 10 and 16 percent among children with one schizophrenic parent (no significant difference has been found in the incidence of disorder in the offspring of schizophrenic mothers as compared to schizophrenic fathers) and a rate of 35 to 44 percent among children if both parents were so diagnosed (Rosenthal 1966). The only potential subjects known to have higher vulnerability rates for the disorder are the monozygotic co-twins of schizophrenics, an obviously much smaller and less diverse group on which to base large-scale prospective research.

All but one of the high risk projects examined in this review were concentrated upon the children of schizophrenics. Two of these involved dual-mated groups (a project conducted by S. Mednick and F. Schulsinger at the Psychologisk Institute in Copenhagen, Denmark, and a project under the direction of L. Erlenmeyer-Kimling at the New York State Psychiatric Institute in New York City), whereas the others focused on single-parent groups. The only large-scale project using another high risk population was one being carried out by E. H. Rodnick and M. J. Goldstein in Los Angeles, which draws on children who are patients in the UCLA Psychology Clinic.

The research designs of these high risk projects have been subjected to scrutiny in the competitive reviews imposed by NIMH. In addition, the overall quality of the research in this field has been enhanced by NIMH efforts to facilitate communication among the researchers in the field and to help them establish contacts with useful consultants on various aspects of their research. The only aspects of the current NIMH grant support system that raise special ethical issues here are those related to financial restrictions. Because of funding limitations, some meritorious projects may have had to settle for smaller samples, fewer tests, and a less adequate number of controls than the principal investigators would have wished. A reading of the available literature does reveal instances of such adjustments, but it is unclear whether the modifications took place during discussions and negotiations on merit or on financing, or whether they took place before or after an initial disapproval of the project. For example, the original Mednick-Schulsinger study in Copenhagen was designed to examine from 800 to 1,000 subjects. The project actually funded by NIMH cut the number of subjects involved to somewhat over 200 (see Mednick 1966).

The other major project in which design was apparently influenced by financial considerations is one conducted under the leadership of L. C. Wynne at the University of Rochester in Rochester, N.Y. This very expensive project (7 years of support at a total cost of $1,414,810) does not have a normal control group. Normal controls were included until the last revision of the application and were then removed because of the time and expense involved in their study. It should be noted, however, that the project does include a control group of neurotic-depressive mothers, and it is indicated that, if at a later time a normal control group appears warranted, a request will again be made to include it. The failure to use normal controls is not so serious an ethical problem in the Rochester project as it could be, since the research is essentially observational in nature and does not involve risk to subjects through clinical intervention.

Another aspect of the design of the Rochester project also involves considerations of savings in time and expense. This is the so-called "convergence strategy" under which the longitudinal aspects of the investigation are substantially contracted by using overlapping groups of children at different ages rather than following one group for perhaps 20 years. First suggested by Bell (1953), the method has as yet been applied only to studies of intellectual development and not to psychopathology (Schaie and Strother 1968). In the Wynne project, certain intermediate outcomes will be substituted for the long-term observation of actual schizophrenic breakdown in the subjects. The convergence strategy here adopted seems ethically unobjectionable. The saving in years of observation, and thus
exposure of subjects, is substantial. Also, the acceleration in producing results from the study could mean faster application of methods of prevention and treatment of schizophrenia.

**Continued Financial Support: An Ethical Obligation**

An important ethical issue that should be noted is the obligation of the sponsor, the Federal Government, to persevere in continued support of the projects over a long period of time. Until very recently, when the Federal Government began to make efforts to cut back on funded projects, there was an expressed governmental attitude of an ethical obligation to support ongoing projects, subject always to congressional appropriations (Kidd 1959, pp. 112-116). No distinction was made, however, between types of projects. All ongoing projects were treated the same, whether involving training or research, and regardless of the research design. We suggest that the highest priority should be given to continuation of support of long-term prospective research projects. If this is not done, the support of earlier years is virtually wasted and the involvement of human subjects is sacrificed to financial considerations in an ethically unjustified manner.

**Study Populations**

Recent hearings in Congress and protests of community groups have called attention to ethical problems in the selection of study populations for research. Protests have related to the overconcentration of some studies on racial minorities, the poor, and such "captive audiences" as mental hospital patients and prison inmates. Are the high risk schizophrenia studies vulnerable on these issues?

When viewed as a whole across the country, these studies are not overconcentrated on racial minorities. In fact, nearly all of the studies are heavily weighted among white subjects. Surprisingly, only a project conducted by E. J. Anthony at Washington University in St. Louis, Mo., involves any significant number of nonwhites. In this project, an effort was made to build a sample evenly divided between white and black subjects, but the group under study is currently two-thirds white and only one-third black. At least two of the projects (Erlenmeyer-Kimling in New York City and Wynne in Rochester) exclude nonwhite and non-English-speaking subjects.

In socioeconomic distribution, the projects are quite varied. The projects in Denmark (national in scope) and in Rochester (broadly regional among all population groups) use a very wide population range. The Los Angeles study of Rodnick and Goldstein draws from a relatively high social and educational level, focusing on the patient population of a university clinic. Projects in New York City, Boston, Pittsburgh, and St. Louis, however, draw their young subjects from among the offspring of present and former patients in State hospitals and public mental health clinics. The majority of the patients in such institutions are from the lower socioeconomic classes. The selection of study populations from among such groups for the projects being conducted in New York City, Boston, Pittsburgh, and St. Louis can be justified essentially on the basis that other more broadly based groups would be very difficult to discover in these cities.

If the children of schizophrenics are to be the focus, and if families with at least one schizophrenic parent are to be studied, then contact must be made largely through the public institutions that treat such patients. Furthermore, these studies are directly related to the disease for which the parent was being treated at the institution. (The proposed new regulations of the National Institutes of Health would limit the use of mental patients to research concerning their own disease, aspects of institutional life, or information that cannot be obtained from any other subject.)

**Informed Consent**

The obligation to obtain a subject's informed consent is firmly rooted as the keystone of the protective safeguards of ethical research. It is the first commandment of the decalogue of the Nuremberg Code. Most of the current interpretation of the obligation comes, however, from medical malpractice cases concerned with medical care, not with experimentation. In fact, the very term "informed consent" comes from the malpractice cases, not from codes or regulations on clinical investigation.
All of the high risk studies follow the HEW guidelines (Department of Health, Education, and Welfare 1971) regarding the obligation of informed consent. Under these guidelines, investigators must obtain the informed consent of the parents—both parents—for the parents’ involvement in the studies and for observation and testing of their children.

The first issue the investigators encounter is the legal capacity of the parents to consent. The problem arises in those projects in which at least one parent is or was a diagnosed schizophrenic. Such a parent could be found mentally incapable of understanding the research and its implications. However, the American law does not automatically deem all schizophrenics incapable of giving an informed consent. The situation is examined as a question in fact, depending on the sickness of the person and the complexity of the required understanding (Lindman and McIntyre 1961). The capacity to consent can exist even when the person is hospitalized and acutely ill. There is less question of capacity, however, if the person is in remission and living at home. The informed consent of a schizophrenic parent is presumed to be valid until a court holds otherwise.

In the projects in which one parent was schizophrenic, the involvement of the children in the research was most effectively assured by gaining the consent of the well parent. These parents may often be under great strain because of the circumstances of chronic mental illness in the family, and care must be taken in seeking the consent of such parents not to manipulate this very situation in order to gain consent.

In all of the studies with only one schizophrenic parent, it was found that consent was being obtained from the well parent and also, whenever possible, from the schizophrenic parent, whether or not he or she was then hospitalized. If the schizophrenic parent was the mother and was then at home caring for the children, the investigators invariably sought her informed consent and full cooperation; if refused, they would not include that family in the project. The legal capacity of the mother to give an informed consent was quite secondary in these cases. The basic consideration was the need for the mother’s aid in encouraging her children to cooperate in the study, getting them to appointments, etc. The investigators might make more than one attempt to gain such a mother’s cooperation, however. We were told of an instance in which a first visit to the home resulted in a total rebuff by the mother. The staff member then talked with the father, gained his consent, and returned another time to talk with the mother. This time she was more amenable to the request and agreed to cooperate. If she had not, no further efforts would have been made to involve the family. Also, in all projects, the parents are free to withdraw themselves and their children from the project at any time.

In the two-schizophrenic parent studies, the issue of legal capacity is, of course, more acute. We were not able to examine the Denmark project of Mednick and Schulzinger, but Erlenmeyer-Kimling, in her New York City project, is careful to obtain her own clinical assessment of the current mental status of both parents and their capacity to understand the explanation provided and to give an informed consent. No family is entered in the study unless at least one parent is found capable of giving informed consent and does so.

All of the studies rely upon parental consent to authorize the involvement of minor children in testing and evaluation. This practice is valid under current American law and the HEW guidelines. Parents are authorized to consent to treatment and to clinical investigation when the involvement is directly beneficial, or potentially directly beneficial, to such children (Curran and Beecher 1969). These projects can all be considered directly beneficial because of the high vulnerability of the children to schizophrenia and the potential advantage of problems being discovered and brought to the attention of the parents. Instances were found in which problems were discovered (a case of epilepsy, for example) and referrals made for immediate help. Also, parents do tend to ask the investigators and their staffs for all sorts of advice, clinical and non-clinical, regarding the children and themselves; seeking advice and assistance is one of the built-in facts of such long-term studies, since the families come to know the research staff much better than is possible in short-term investigations and rely on them as a source of professional support. This reliance is most apt to occur in clinically oriented projects where the staff is composed of clinicians. In a study conducted at the Massachusetts Mental Health Center, it was found that discharged patient-parents very often relied on the periodic visits of the nurses in the study as their only source of follow-up care (Nelson and Grunebaum 1972).

We did not find that the projects were using formal procedures (i.e., signed consent forms) to gain the informed consent of the children themselves.
At our suggestion, some of the projects that we site-visited have adopted such a procedure with all teenage children. A recommendation was made (Curran 1973, p. 141) that all investigators be required to obtain the informed consent of all high risk children and children used as controls from the age of 14 and older (Curran 1973, app. III). At the time this recommendation was made, it was not a clear legal obligation, but it is supported by important American case law and the American Law Institute (U.S. Department of Health, Education, and Welfare 1973a, sec. III, D, 3). The age of 14 was selected rather arbitrarily, since the cases do not provide any specific age. The legal test is an individual one, dependent upon the intelligence and maturity of the child. Since our recommendation was made, the proposed regulations of the National Institutes of Health would require informed consent of all children 7 years of age and older (U.S. Department of Health, Education, and Welfare 1973a, sec. III, B). This very low age level has no support in current American case law or statutes, and no authorities are cited in the proposal.

It should not be inferred from the above that the researchers conducting high risk studies do not explain their investigations to the children. Depending on the age of the child and the procedures employed in the particular study, they do inform the children of their intentions in the study and explain the procedures to be used. Quite obviously the cooperation of these youngsters is necessary. They must keep appointments and must often engage in rather complex physiological and psychological testing that sometimes requires the greater part of a day. It was indicated that the research staff tries to answer all of the children’s questions truthfully and completely. We doubt that any of these investigators would resist, in any way, a requirement of formalized “informed consent” of children. In fact, in one study, when we suggested the advisability of seeking formal consent from teenagers, the principal investigator indicated that he would include the younger children, allowing them also to sign such forms in order not to “leave out” anyone in the family group. (Any parent should be able to recognize that problem, we observed!)

Children as Research Subjects

Earlier in this paper we called attention to the fact that the use of children as the primary focus of research was a critical ethical issue in these projects. Since the issuance of HEW’s proposed new regulations, this factor has assumed even greater importance. Section III, B of the new regulations would require not only parental consent and the consent of the children themselves at age 7 and older but would require what is called “supplementary judgment” by an ethical review board of the HEW sponsoring agency and an ad hoc “protection committee” set up by each research project at its own institution.

Section III, A of the proposed regulations summarizes well the limitations on the use of children in research, with which we are in basic agreement. When the risk of a study is negligible and the potential benefit is “explicit,” the proposal asserts that the use of children is not ethically barred. When risk cannot be measured by prior animal studies or studies in adults, children should not be used as subjects. When the risk seems to be more than insignificant, the potential benefit must, according to Section III, B, 3 of the proposed regulations, be such as to “far outweigh that risk.”

At the present time, before the application of any means of therapeutic intervention, all of the high risk studies comply with these new proposed regulations because they are essentially observational in nature, using only standard physiological and psychological tests on the children. None of these tests involves any significant risk. The proposed regulations make a specific reference to the need to gather “full understanding” of child growth and development, metabolism, and biochemistry. It is acknowledged that these processes can be studied only in children. Furthermore, it is recognized that certain diseases and modes of therapy can be studied only in humans. Schizophrenia is one of those diseases.

The Issue of “Labeling”

The most serious problem related to informed consent and full disclosure in these projects was the widespread reluctance of the investigators to disclose to the parents or to the children the actual statistical vulnerability of the children to schizophrenia. There was a distinct fear that to do so could jeopardize the children and cause further emotional trauma in an already stressful family situation. Most particularly, there was a resistance to indicating that the vulnerability had, or might have, a genetic origin. The resistance here was due, first, to the
lack of adequate scientific support for such a statement. Current research provides primarily epidemiological evidence of higher vulnerability in the children of schizophrenics. Also, it was felt that the families would be more devastated by being told that the disease might be inherited than by being told that children in the home of a schizophrenic parent or parents could have emotional problems due to their disturbed home life.

Part of the reluctance to disclose the statistical vulnerability to schizophrenia of the subject children is also related to the fact that many of the projects do not have the resources to provide emotional support for the children and families who might be adversely affected by such disclosures. None of the investigators in the projects indicated that they would deliberately mislead the families. If pressed with very specific questions, the principal investigators interviewed said they would disclose the entire risk factor.

The high risk projects provide very full descriptions of the research procedures to be used and the reasons for selecting the particular children under investigation as subjects. The fact that the children were selected because they are the offspring of schizophrenics and are living in such a home atmosphere is fully disclosed. An example of the consent form used in one of the studies follows:

I consent to participate in the [named] Child and Family Study. I understand that this study is concerned with learning how families such as mine cope with emotional disorders in a parent and how this may affect the development of children in my and other families. Participating parents and children will be interviewed and tested, both physically and psychologically. I understand that there are no known physical or psychological hazards to any of these tests. Some of the interviews and tests may be recorded on sound tape or videotape. All materials will be kept confidential but may be used for professional, educational, and research purposes. Under no circumstances will my name be associated with any information transmitted about these studies. If I so desire, I may, by specific written permission on another form, allow the Principal Investigator to use any recognizable material for professional publication and for my own medical care and treatment. All of my questions have been answered satisfactorily, and I understand that I am free to withdraw from this study at any time for any reason whatsoever.

This is the entire statement, though the staff will also answer further questions truthfully if they are asked. It should be noted that the statement expressly mentions that the research relates to learning how the emotional disorder of the parent may affect the development of the children.

In another project where participation is sought through a letter sent to the parents, the purposes and procedures are even more fully spelled out:

Dear [Name]:

We are writing to ask you and your family to take part in an important research project sponsored by the National Institute of Mental Health and the [named] Psychiatric Institute.

This study is concerned with families in which a parent has been hospitalized for emotional illness. We appreciate that, as members of a family that has experienced an emotional illness, you will have had to face a great deal of stress. We believe, however, that with your help our project will contribute greatly to a better understanding of the needs and problems of families such as yours. We hope to develop programs in the future to meet these needs, so that other families will have to undergo fewer difficulties.

What we are asking of you is that you and your children spend two or three hours talking with us in your own home (or at our offices if you prefer). We have found that this visit usually turns out to be a pleasurable experience for the families that are assisting us.

We will also want to arrange with you for your children to visit our offices for a few hours of tests and other activities. We know, from the number of families that have already participated in the project, that children find their day's visit interesting and enjoyable. We arrange for transportation between your home and our offices, and return. A description of the children's day is given on the attached sheet.

We assure you that the information you give us will be treated in strictest confidence and will be kept in locked files available only to qualified professionals and their research associates on our staff. The information that we are obtaining on a large number of families will be used for statistical purposes only. You and members of your family will not be identified by name at any time.

Within the next few days Dr. [Name] will phone you. He/she will answer any question you may have and will make specific arrangements with you for your participation. Although you will find your part in the project to be a pleasant experience, we understand that it may be somewhat of an imposition on your time. In recognition of this and to express our very great thanks for your help, we would like to send you a [check] check as soon as your children have visited us.

Because of the importance of the answers that we
Here again the vulnerability factors are not quantified, but mention is made of the "great deal of stress" experienced by a family when a parent has been hospitalized with emotional illness. Is this an ethically adequate disclosure?

The current HEW guidelines (Department of Health, Education, and Welfare 1971) on the requirements of informed consent are as follows:

1. A fair explanation of the procedures to be followed, including an identification of those which are experimental;
2. A description of the attendant discomforts and risks;
3. A description of the benefits to be expected;
4. A disclosure of appropriate alternative procedures that would be advantageous for the subject;
5. An offer to answer any inquiries concerning the procedures;
6. An instruction that the subject is free to withdraw his consent and to discontinue participation in the project or activity at any time.

The above criteria would seem to be met in the high risk projects described. The risks of the testing procedures are fully disclosed. The guidelines do not require that the subject be told all of the underlying hypothesis upon which the research is posed. If a research project is therapeutic in nature, the guidelines specifically allow "a certain amount of discretion" to be used in withholding full information on risk, taking into account the patient's emotional condition. In nontherapeutic projects, no such discretion is allowed, and full disclosure is required. It is indicated that the subject must be told all the facts, probabilities, and opinions that a reasonable man ought to consider before giving his consent. However, the context again seems to be related to the risks of the study itself, not the underlying hypotheses upon which it is based.

There can be instances where holding back information about matters other than risk could influence whether a subject would participate in a study. An example would be the whole-body radiation studies sponsored by the U.S. Department of Defense in order to provide information about the effects of hydrogen bombing. In an Ohio project, terminally ill cancer patients were asked to consent to experiments on whole-body radiation, but were not told of the war-related purposes or the Department of Defense sponsorship. It can be speculated that some patients might have refused participation had they known these facts, even though they had nothing to do with the risks of the procedure itself.

Section I, K of the proposed new regulations of NIH would require that subjects be informed fully of "the nature and purpose of the research and the procedures to be used." Would this new definition change the obligation to reveal the statistical vulnerability of the high risk subjects? Is such information an essential part of revealing the nature and purpose of the study?

It would seem necessary that the researcher reveal the reason for studying these children, and this would require telling parents and children that they are being studied because of their vulnerability to mental disease. The discussion of the reasons for vulnerability becomes difficult due to the very lack of scientific information on the disease's etiology. The subjects can be told that the project is exploring both environmental and genetic factors, with the stress on the former in the studies themselves—a statement that is uniformly true at the present time. At this stage, the revelation of statistical vulnerability may be irresistible, due to the subjects' fears that their chances may be even higher, or may be inevitable, of coming down with the disease.

The latest trend of American court cases of informed consent in clinical medical malpractice also supports an expanded requirement of full disclosure. The key cases are *Canterbury v. Spence* in the District of Columbia and *Cobbs v. Grant* in California. In the *Canterbury* case, the court asserted that all information material to a reasonable decision must be furnished, and concluded: "The physician's privilege to withhold information for therapeutic reasons must be carefully circumscribed." Both *Canterbury* and *Cobbs* rejected the test of

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"accepted practice" of other physicians as the criterion for the scope of the obligation and held that the jury could determine the physician's duty as a matter of fact in each situation.

**Labeling Outside the Home**

Every effort is made in the high risk projects to avoid attaching any vulnerability label to the target children in schools or other settings where they may be observed or tested. In the schools, information on why the children were selected for study is given only to high-level officials who are not in direct contact with them. At the schools, the investigators give teachers limited information, disguising the target child among two or more controls, or among an entire class. The teachers are told the purposes of the study as it relates to the tests and observations conducted on site at the schools, but usually not about the relationship to severe mental illness. The same practices are followed where target children are seen in general hospitals or mental health clinics.

Avoidance of labeling target children cannot be continued if some of these projects, or new projects later begun, add specific therapeutic intervention applied in the schools. In such situations, as discussed later in this paper, the possible detrimental effects of labeling would have to be weighed against the potential benefits of the intervention.

It should also be noted that these efforts at sheltering the target children from labeling in the schools are often much less compelling in reality than in theory. It has been found by some researchers that the teachers were already aware that the index child had a schizophrenic parent. However, the same teacher might also know that other children had serious problems at home, such as divorced parents, a mother who committed suicide, a father in prison, or a brother on drugs. Also, it was found that many of the teachers had already had trouble with the index children in class. Without being asked, the teacher sometimes picked out the index child among a group as the "real" object of the study because of this experience. Findings in projects now under way indicate that many index children are having noticeable trouble in school (Rolf 1972 and Watt 1972a).

**Access to Patient Records**

In many of the high risk studies, the researchers examine patient records in mental health facilities. In most of the projects, the records were examined only to find suitable schizophrenic patients: those with children and living in the geographic area where the study was being conducted. In these studies, permission of the patient was not sought to examine the records in this cursory manner. Permission was legally accorded by the institutional authorities to reliable researchers who were obliged to assure confidentiality in their research (Curran 1973, app. IV). After the names of the patients were obtained, informed consent was sought for involvement in the studies, as previously indicated, where parental interview and child observation and testing were to be done. The consent form and letter to parents included on earlier pages of this paper are examples of the procedure followed in such studies.

In a followup study of former psychiatric patients, Nelson and Grunebaum (1972) expressed concern about the manner of making contact with the patient and revealing their awareness of the person's prior psychiatric history. In this study, not a high risk project, the authors indicated that some ex-patients contacted by telephone "plunged immediately into an emotionally stressful experience. One woman became progressively psychotic as she reviewed her feelings over the telephone" (p. 1359). If former patients were known to be under psychiatric treatment or medical care, Nelson and Grunebaum indicated that they contacted the physician rather than the patient concerning followup information on the grounds that:

It was our considered judgment that it was more ethical to avoid patient distress by contacting the professional than to ask first for consent of each individual patient, particularly those who had not received treatment recently. [p. 1360]

Nelson and Grunebaum suggest that teaching hospitals seek consent of all patients to engage in followup studies at the time of their admission or discharge. They suggest that, in clinic or emergency-room cases, the consent be made a part of the consent for treatment. (The particular followup study being discussed in the paper involved wrist-slashing cases where emergency
admissions were apparently frequent.) In conclusion, the authors said:

It also should be explained clearly to the patients that to accept and authorize treatment at a teaching hospital carries with it the specific provision for later follow-up. This obviously can be a problem where there are no readily available alternative facilities. [p. 1362]

The suggestion of Nelson and Grunebaum may be in accordance with traditions in teaching facilities, but it is highly doubtful that the current American courts and civil-liberties-oriented patients’ rights groups would take kindly to this approach. An important California case has said that patients in teaching hospitals have no obligation to submit to being teaching or research subjects. The suggested method of obtaining consent has too much of an air of coercion about it. In the case of an emergency-room or any psychiatric admission, the validity of such a consent would be highly questionable because of the stress under which the patient can be assumed to be at that time. In a public mental facility, which most psychiatric facilities in this country are, patients have free access to needed care, and no such conditions could be imposed unless authorized by statute. Even the statutes might be invalid constitutionally as an unreasonable abridgment of the free access to care.

On the other hand, efforts to obtain a patient’s informed consent after the time of discharge but before the patient has physically left the grounds probably would not violate ethical or legal principles, as long as the consent could in no way be interpreted as a condition precedent to the discharge itself. The discussion would then be appropriate as an indication of the hospital’s concern and interest in the future health of the patient.

In one of the high risk studies, the investigators were faced with the kind of problem discussed in the above paper—the possibility of damaging patient contact. The study was designed to be conducted with children in the schools and did not involve parent interviews. Access to suitable child subjects was, however, to be obtained from the records of patients of mental health facilities. The names of suitable patients, those with children in certain age limits and living in particular areas, and the names of the children of the patients were to be obtained from certain psychiatric hospital and clinic facilities. The patients’ approval was not to be obtained prior to record examination or receiving the names of suitable parents and children. Permission would be sought from these same parents when their children were to be observed and tested at the schools, but such permission was to be sought at the same time from parents of a group of normal controls, who were to be used partly to avoid labeling the index child. At that time, all of the parents in the total group would be told only about the purpose of testing their children with regard to psychological and social adjustment to school. This was the true purpose of the study and all tests were to be indicated. However, the index cases were not to be told that they were specially selected because of the parents’ prior psychiatric history.

When the research proposal was first reviewed, the human studies committee of the researcher’s institution was of the opinion that the informed consent of the parent-patients should be obtained prior to examining the records and receiving the names of patients and their children. The researcher initially agreed to this condition for approval of his project, but after the committee meeting he became more and more concerned about the potential detrimental effect upon the parent-patients. He consulted not only his own psychiatric associates in the study, who had had long experience with schizophrenia, but a number of other experienced and highly regarded researchers in the field and other experts in schizophrenia throughout the United States. Without exception, these clinicians and clinically trained researchers warned against alarming ex-patients with a full explanation of the project at so early a stage in the research. They were concerned about possible paranoid ideation. This reaction could take the form of patients’ fears or guilt feelings concerning themselves or their children in a situation where no continuing psychiatric contact was planned with the families. The researcher then went back to the human studies committee and asked for reconsideration of the condition. He indicated that he believed the possible damage to the patients to be so great that he would abandon the project rather than accept this requirement. On reconsideration, the committee reversed its earlier decision.

Even with this condition removed, however, we are still left with the question of whether the index parents should have been told at the later time (when they were

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*Tunkle v. Regents of University of California, 60 Cal. 2d 92, 32 Cal. Rep. 33, and 383 P. 2d 441 (Cal. 1963).*
asked to permit observation and testing at school) that their children were the primary focus of the research because they were the offspring of schizophrenics. In some high risk studies, as noted earlier, this is done. As we have also noted, the new proposed regulations and new court decisions might require informing the parents and children of the statistical risk of schizophrenia.

Access to School Records

School records are examined in many of the high risk studies to see how the index children are progressing. Some of the researchers limit their investigation to record examination. Some also ask questions of teachers and students in the class where the index children are located. None of the latter ask only about index children but about a group (usually three pupils) or about the entire class.

One high risk researcher (Watt 1972b) has written about the use of hospital and school records and has commented upon ethical aspects of the subject. He has suggested that the use of mental health department patient records to find schizophrenic parents and then the extensive perusal of their children’s school records from early childhood through high school, with particular attention to the individual evaluations of the children’s personal, psychological, and social development by the teachers, can be a very useful and much less expensive method (in time, manpower, and finances) of assessing the progress of high risk children than current methods. This use of records could also provide a method of drawing larger samples from a wider universe. He suggests that this type of “unobtrusive” study should be ethically justified without seeking the permission of the parents to examine either their own patient records or the records of their children in school. He would rely on the permissions obtained from the mental health authorities and from the local school authorities at the highest level. The classroom teacher would be kept unaware of the fact that the research was focused on the children at risk, or that the genetic-risk children were of special interest. (Presumably, Watt intends that all of the classroom records would be examined, or a triage method would be used.)

Watt (1972b) considers this approach to be ethically proper because the research participation of the parents and children is “so indirect and minimal as to approach historical research in which the public or recorded acts of a person are studied without his consent being thought at all necessary” (p. 12). He expresses his concern, as in the consent situation related earlier, that informing patients of the full purposes of the study would unnecessarily alarm them about the possible vulnerability of their children to mental illness.

Watt also defends his position on access to the records without consent of the subjects on the basis that...

... when the research participation is as minimal as this, I believe that society’s right to know outweighs the limited invasion of privacy for these individuals. In the efforts to reassert the rights of individuals in these ethical matters I have heard little said for the rights of society, which everyone seems to agree bears the primary burden in the case of schizophrenic outcome. Among these rights of society I should like to include the prerogative to monitor in a reasonable way the physical, social and intellectual development of children. [p. 12]

Watt’s arguments are quite persuasive, and the benefits to be derived from such research could be substantial for society. Many legislatures have authorized supervised access to patient records without patient consent when the information is used for research purposes, the data are kept confidential, and publication is in aggregate form only. The legislation is usually not very detailed, allowing wide discretion to officials in charge to permit access to competent and ethical researchers. Dr. Watt, however, was also advocating quite extensive access to school records. Here, statutory authorization has not been so widespread and open-ended as in the medical field. Some States allow use of school pupil records for research, whereas others are silent on the matter.

Gallant and Grunebaum (1972) have expressed their concern about the ethics of observational research:

What is the right of people to be unobserved in their lives, even if they do not know that observation is occurring and the observation is in no way harmful? Should we conduct unobtrusive observation which our subjects might not consent to were they asked to give consent?

Gallant and Grunebaum, both experienced in high risk research, give no answer to their query, but they are obviously bothered by it. In a personal interview, Dr. Grunebaum added that he was particularly concerned with such observational studies when the research involved no direct benefit to the families or the children,
such as some psychiatric consultations or treatment intervention.

An analysis of these issues must involve a clarification of what is meant by "observation." A single examination of records in a retrospective way, as in the Watt proposal, may be the most minimal type. Longitudinal "observation," even if only of school records over a period of years, would seem to be more obtrusive, especially if it accumulates more data than would be available in any one source. The observation increases in intensity if the schoolteachers are asked to make a new and independent assessment of the children solely for the purposes of the project, or if a research staff member does the observing and recording of conduct. A broader observational measure is applied if the index children's classmates, along with the index child, are asked to rate each other in something like the Bower (1960) play-casting exercise.

When it comes to the more obtrusive observational measures (or "monitoring," as Watt terms it), Watt (1972b) asserts that he is "willing to concede to the discretion of the parents on one point: any parent should be permitted to exempt his child from an assessment procedure he finds objectionable" (p. 13). Dr. Watt further qualifies this concession, however, by suggesting that the school authorities make a "general announcement" to the parents and allow the parents to request further information on what procedures are to be used and to request that the child be omitted from any test found objectionable. Thus, as he admits, the burden is placed on the parents to take affirmative action—first, to find out what is going to be done to their children, and then to object to any specific procedures involved. Otherwise, the only choice the parent would have would be to refuse cooperation on the entire program included in the general announcement, no matter how broad or vague it might be. To illustrate his idea, Watt suggests a hypothetical case: In a "routine blood test" in the sixth grade, the research team might ask the school authorities to test for the Frohman plasma protein factor in all children. The parents would apparently get the general announcement of a blood test (or of a general physical examination with no mention of a blood test?) and could object to the taking of blood on "personal, moral, religious, medical, or other" grounds. However, the objection would not be to the taking and recording of genetic information, since under the Watt principle they would only be told about it if they made further, uninvited inquiries that would reveal this additional procedure and its purposes. Permission would be granted to the researchers solely by the school authorities (and here he adds the medical personnel who would do the blood test and stick the children).

At the conclusion of these suggestions, Watt (1972b, p. 13) expresses the hope that it will soon be possible to conduct "universal surveys of general variables" in entire school systems from which retrospective sample groups could be drawn for different research purposes. He asserts that it would be "grossly impracticable" and "ethically unnecessary" to obtain parental consent for each individual.

Dr. Watt's paper is a cogent statement of the researcher's position. In the present political climate of concern for privacy, however, with emotional outcries against almost any use of records without the person's consent, it seems doubtful that a legislative body would go beyond current practices and authorize "monitoring" of an extensive type in the public schools without explicit parental consent.

**Therapeutic Intervention**

At what point, if any, is there an ethical obligation to intervene therapeutically in the lives of children found prone to a serious chronic disease such as schizophrenia? The principles of ethics, social and medical, contain few positive duties. Most of the principles are negative in that they set boundaries beyond which the just should not venture.

The positive or activist responsibility of the scientist is to the seeking of truth. In high risk studies, this responsibility is fulfilled in continuing efforts to find the cause or causes of schizophrenia and in learning more about child growth and development. Most of the high risk studies are in areas of fundamental research. When does the medical duty of clinical investigation become significant? C. J. Wiggers (quoted in Beecher 1959) has observed: "...among experiments that may be tried on man, those that can only do harm are forbidden, those that are harmless are permissible, and those that may do good are obligatory" (p. 463). In the high risk field, Garmezy (1971) has put the question well. He asks,

Finally, what can be said about the issue of intervention? A conservative viewpoint would hold
that intervention, in the absence of knowledge about the process of pathological development, would be premature. And yet the ethical demands placed upon those who study high-risk children can be a powerful force that compels one to look, perhaps with hesitancy, upon the necessity of intervening irrespective of one's confidence in the tools that are available for efforts at prevention and containment. [p. 113]

In nearly all of the high risk studies at present, I would say that there is no affirmative obligation to intervene which can be spelled out in clear terms. Most of the projects are in the observational category and the index children are not patients. However, the projects are close to clinical orientation in that they are focused on a particular disease to which the children are vulnerable and they often involve a patient, the parent, who does have the disease.

We would see in these projects two types of issues of ethical responsibility to intervene. One would relate to answering emergent problems in current projects. The other would occur when the scientist-clinicians discovered enough information applicable to prevention or treatment that their duty to intervene therapeutically became strongly felt.

The first type of ethical obligation has arisen in some of the current projects. The investigators, in the course of testing or observing the children, have discovered severe malfunction, have alerted the family to this fact and have advised them to seek help for the child. In another project, observers were placed in the home. Although the observers were expected to be passive in the fashion of scientific research, they were, inevitably, asked to help the family in many different ways and did, in fact, provide assistance.

When more basic information is discovered within the project, however, the question of experimental intervention is of a different order. To answer the question of ethical justification, we must examine the research strategies of the various high risk studies. I would describe two predominant themes in the inquiries, one seeking predictors of vulnerability to the disease and one attempting to determine criteria for intervention. For example, I would call the identification of complications in pregnancy and childbirth, including low birth weight, a criterion for intervention. It was first noticed by Mednick et al. (1971) among schizophrenic mothers and their children in the Danish project. At the University of Rochester, Sameroff (cited in Mosher, Gunderson, and Buchsbaum 1973, p. 26) studied the same period in schizophrenics, neurotic depressives, and normal controls and found significantly more delivery problems in both disturbed groups. The children also showed more abnormalities. It was tentatively concluded, therefore, that these findings do not indicate that these complications are specific for schizophrenia. I suggest the Sameroff study does confirm that perinatal problems are criteria for intervention. Such criteria do not require the specificity of predictors of vulnerability. Improved prenatal care of schizophrenic mothers and changes in obstetrical practices at childbirth could affect the prevalence of schizophrenia and other disorders in children who now may be damaged prenatally and at birth.

The dominant strategy for locating predictors of vulnerability is the "continuity approach" in which the investigators search for similarities in the reactions and behavior of high risk children and adult schizophrenics (Neale and Weintraub 1972). Mednick and Schulsinger (1972) have worked with certain psychological and physiological factors, and Erlenmeyer-Kimling has also been examining such factors. Anthony (1972, p. 392) has concentrated on more clinical, psychiatric diagnostic, or symptomatic factors which, in the children, he calls "microepisodes," or prepsychotic trends in transient miniature (microparanoia, microhebephrenia, and microcatatonia). The continuity approach is useful at these early stages in research because it provides ready hypotheses for investigation. However, it is essentially a retrospective analysis in which what is thought significant in adults is traced back in children. There is no way to tell, even when the factor is found, whether it is a symptom of the disease or a precursor of it. In Anthony's work (1968, p. 311), the analysis seems clearly to indicate the symptomatic nature of the factors under investigation. He speaks of a "gradual accumulation of disturbance that continues progressively throughout the child's development." It makes no difference whether a particular factor is causative or symptomatic, however, if the factor is looked at merely as a predictor. The important point is its accuracy and specificity in selecting out the children who will, if something is not done, break down later with full-blown psychotic disease.

In those studies in which criteria for intervention are discovered, the move from observation to intervention is natural and direct. The ethical justification to begin
Experimental work will depend on the confidence level of the findings and the feasibility of a particular intervention program in addressing the problem. Intervention could be preventive, as in the perinatal area discussed above, or more therapeutic in nature. An example of the latter would be those high risk projects designed to examine stimulus overload. The theory is that particularly vulnerable children will evidence a loss of inhibition in incoming sensory signals either by the reticular activating system, or by hippocampal dysfunction, or at the cortical level. Various tests are being conducted on these children in more than one project we site-visited to see if such incapacities can be demonstrated. If so, intervention techniques can be addressed to helping these children screen out stimuli and avoid sensory overload.

Different issues are raised in research that seeks predictors of vulnerability. The aim here is to select out the most vulnerable children in the already high risk group of children of schizophrenic parents. The Anthony (1968) project in St. Louis is the primary example of such an approach. A quantitative scoring is applied to each child. The scale includes "inherited, reproductive, constitutional, developmental, physical health, environmental, and traumatic risk." The key to success here is the degree of accuracy in predictors and the stage of life of the child when the accepted level of accuracy of identification is achieved.

**Psychotherapeutic Intervention**

The least problematic of the proposed methods of therapeutic intervention are those that would use quite standard psychotherapeutic methods on subjects already manifesting some symptoms of emotional and behavioral disorder. There do not seem to be significant risks or inconveniences to the patient-subjects in these methods, as distinguished from other techniques such as the use of drugs or behavior modification.

In the Anthony (1968) project, which is based in a child psychiatry clinic, the objective has been to search out clinical diagnostic or symptomatic factors that provide a continuity of psychopathological development. The project involves both a crisis intervention program and a so-called precrisis program.

This psychotherapeutic approach also applies to a project such as the Rodnick and Goldstein project in Los Angeles, in which the high risk children are selected from among patients of a psychology department clinic in a university setting.

**Drug Intervention**

The possibility has been raised that psychotropic drugs might be used experimentally over a long period of time with certain high risk children who display subtle psychophysiological disturbances that have been identified as criteria for intervention. These drugs would be used to dampen down such disturbances at young ages in the hope of interrupting the development of serious mental disease.

In our opinion, this type of drug intervention cannot be justified ethically at this time. These drugs have recognized side effects of a serious nature, varying with the agent used, and have dangers in long-term use that are now being discovered and measured (Shader and DiMascio 1970). These dangers could be particularly aggravated if drugs were administered on a sustaining basis beginning in early childhood. Clinicians have had no experience with giving these drugs to very young children for many years or a lifetime (DiMascio, Soltys, and Shader 1970). Furthermore, the high risk children to be treated, even if selected as particularly vulnerable, would not yet have been identified as manifestly ill or disturbed.

In a high risk project to be conducted by Mednick and Schulsinger on the island of Mauritius, some consideration was initially given to the use of psychotropic drugs as an intervention technique as described above. But in an interview with Dr. Mednick in June 1973, he indicated that this possibility had been rejected because of the detrimental side effects cited above and because the preventive potential of such drugs is not yet sufficiently supported to justify experimental testing.

**Learning Theory and School-Oriented Intervention**

We have not reviewed any specific proposals for the use of operant conditioning in high risk children, but such techniques, if applied, would probably be aimed at developing in high risk children better methods of coping with problems and avoiding stress that might trigger damaging incidents.
Some learning-theory methods might be applied in school situations. For example, the study to be conducted by Mednick and Schulsinger on the island of Mauritius would involve setting up special nursery school classes to be attended by high risk children. There could be considerable merit in such a study, based upon the substantial experience with high risk children that Mednick and Schulsinger have had in their Danish longitudinal study.

Since the Mauritius project was still in the planning stages at this writing, no particular method of providing specialized intervention techniques had been decided upon. We would only suggest at this time that the investigators avoid placing the target high risk children in nursery schools not provided to other children in the same population group, and also refrain from segregating the children in special classes apart from other nursery school classes provided for normal children. Such practices would amount to public labeling of the target children at a very early age in a manner not ethically justified by scientific findings at this time.

Other Interventions

This review of ethical and legal considerations in high risk studies has not, of course, exhausted the forms of intervention possible in the lives of these children. One important form of intervention not discussed in any of the research proposals reviewed is a separation of the children and the schizophrenic parent. There are several means of achieving the separation. The well parent in a single-parent schizophrenic family could get a divorce or separation and keep the children away from the schizophrenic parent permanently or limit contact severely. The children could be placed in the homes of relatives, or in foster care, or could be put out for adoption. The studies by Heston (1966) in Oregon and by Kety et al. (1968) in Denmark have produced important findings on the children of schizophrenics put out for adoption, many at very early ages. The incidence of mental disorder was still quite high in these children, strengthening etiological theories of genetic vulnerability. I do not find any discussion, however, of the positive or at least preventive aspects of separation of different types in reducing even higher incidence. All of these were followup studies. I have seen no proposals for longitudinal studies of physically separated high risk children. Would such studies, if they could be developed, be justified ethically? There are ethical and legal issues raised in followup studies of adopted children of schizophrenics, such as access to the adoption records and any obligation to inform the children of the psychiatric history of their parents. These issues are not unlike those already discussed in this paper.

The work of Anthony (1968) in St. Louis calls attention to the damaging effect on the children of intermittently hospitalized and released schizophrenic parents under current “revolving door” policies at the State hospitals. Anthony suggests therapeutic support programs for such children to help them through those experiences, and he also suggests setting up substations of State mental hospitals to offer comprehensive care and support for the families. Anthony believes that psychotherapy can be used to build a sense of separation and independence in children even as they remain in the home of the schizophrenic. Anthony does, in fact, consider as among the more vulnerable children those who overidentify with the psychotic parent and mimic the symptoms of that parent more than the other children.

It seems unlikely, however, that an experimental project involving the use of separation as an intervention technique could be developed. At most, a project might be arranged to conduct longitudinal studies in cases in which it had already been determined to place children for adoption at birth or shortly afterward.

Another form of preventive intervention would be the counseling of schizophrenics to avoid marriage and having children because of the genetic or environmental risk involved. At what stage of research knowledge would it be ethically justified to encourage such counseling? The literature of genetic counseling is now quite extensive, but the ethical issue of determining when information and advice on specific vulnerabilities should be given to individuals has not received much attention. The counseling programs seem to operate on the assumption that these issues are settled in their own programs in favor of disclosure of the genetic information, leaving the individuals concerned free to decide whether or not the risks are serious enough to cause them to avoid marriage and/or childbearing in the particular situation (Hilton et al. 1973). Judged by other genetic counseling programs, the risk now uncovered for two-parent schizophrenics having schizophrenic offspring seems clearly within the range of disclosure and advice, and the risk is also probably high enough in one-
schizophrenic parent situations to warrant disclosure (Harris and Hirschhorn 1973). The discussion of risk could include both genetic and environmental factors.

The success of any genetic counseling programs in discouraging childbirth and/or marriage, even among mentally “normal” individuals, is still problematic. Evaluation studies (Leonard, Chase, and Childs 1972 and Sibinga and Friedman 1971) of genetic counseling programs indicate that those who are counseled often do not understand the basic information provided about the disease and the risks associated with it. Also, many people who receive counseling on the high risk involved go ahead with childbearing, much to the chagrin of professional geneticists and counselors (Ramsey 1970). Statutory bars to marriage by schizophrenics have been on the lawbooks in many States since the early decades of this century. Twenty States currently have laws in this field that contain enforcement provisions against schizophrenics marrying (Curran 1973, app. V). There has been very little indication that these laws have ever accomplished their purpose. In the past, the main method of preventing schizophrenics from marrying has been long-term hospitalization of those whose disease is fully manifested early in life. The nationwide movement of deinstitutionalization has reduced very substantially even this barrier to marriage. In the future, counseling programs probably will be the main preventive method in both marriage and childbearing. The civil rights movement is strongly in favor of retaining rights of marriage and childbearing in the mentally ill, leaving the matter to individual choice without either legal impediments or coercion being imposed.

Remaining Special Issues in Long-Term Studies

The last area of concern in high risk studies relates to responsibilities inherent in the long-range nature of these projects. I will summarize some of the concerns that were brought out earlier, and add a few other points not raised in the context of other ethical issues.

Special attention was given to the obligation of sponsors of long-term high risk studies to give priority to continued funding. As a corollary, we should note the similar obligation of the researchers to persevere in spite of setbacks in the research and offers of attractive positions elsewhere.

Care should be taken in protecting the privacy of subjects by the methods used to follow up on subjects as the years go by. Very aggressive followup methods may prevent the loss of subjects but can also result in unnecessary exposure of the subject’s family history or raise questions about the person because a psychiatric group is seeking him out.

The recent investigation of the Tuskegee Syphilis Study (U.S. Department of Health, Education, and Welfare 1973b) did not make specific new recommendations concerning long-term studies but did suggest the framework of basic ethical obligations in such research by its condemnations of the shortcomings in that project. The first or primary duty brought out therein concerns the affirmative obligation to keep constantly aware of the implications of changes in scientific knowledge and treatment methods upon the project and its subjects. Closely related to this is the ethical responsibility to intervene and to use this knowledge within the project when it is clearly of direct benefit to the subjects, instead of, in the narrow interests of preserving the original research design, doing nothing.

Other important obligations also relate to the passage of time in the projects. For example, when high risk studies involve children, changes will be necessary as the children grow in maturity, attend school, contemplate marriage, and seek jobs. One rather obvious ethical demand will be to add the formal written consent, on a fully informed basis, of all children as they reach the required age for such consents. I have noted that the very nature of long-term, repeated contacts builds up dependence by the parents and children on the researchers. The projects should therefore develop well-thought-out practices for responding to this dependence.

The passage of time also means the inevitable building up of considerable amounts of information in the projects. Efforts must be made to protect the confidentiality of that information under the specific laws of the jurisdiction where the projects are located. Since the laws differ so much, individual approaches to this problem must be made in each State and for each type of project. (See Curran 1973, app. VI, for a more detailed consideration of these specific legal matters.)

The keeping of confidential records does not mean that the investigators in these projects should take the position of never aiding subjects by releasing certain information from the projects for the subjects' benefit.
In fact, policies should be developed in each project to determine when information will be released.

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