

Proposed Activities of

The Methodist Hospital/Baylor College of Medicine

International Consortium for Research and Treatment of Radiation-Induced Injury

Specific Aims

The underlying philosophy of the proposed studies is based on three propositions. First, the effects of Chernobyl will continue to be seen for the next generation. Second, despite the rapid reduction of tensions related to nuclear war, the reality of U.S. and worldwide dependence on nuclear energy make the reality of future accidents like Chernobyl a high priority concern to the medical community. And third, as a recent emigre from the Ukraine has commented in consulting with our project staff, "radiation effects the whole body, not just the blood."

With this in mind, the broad purpose of the proposed research at The Methodist Hospital/Baylor College of Medicine will be to conduct a set of seven pilot/feasibility studies touching on various disease sites as well as psychosocial sequelae to radiation exposure following the Chernobyl accident. The studies are designed to complement the work of other consortium members. Rather than repeat the classic dosimetry studies proposed for Russia and Israel, a preliminary project will be to begin establishing a U.S. based registry of Chernobyl victims and to gradually phase in the other projects using human measures and biomarkers such as biologic dosimetry.

Background

As part of the Consortium for Research and Treatment of Radiation-Induced Injury, The Methodist Hospital and Baylor College of Medicine bring the combined resources of (1) the largest, not-for-profit, teaching/research and acute care hospitals in the United States and (2) the only private medical school in the State of Texas. Together, the two institutions have joined resources to address many specific research challenges e.g., Cardiovascular Disease, Cancer, Organ and Bone Marrow Transplantation, Cancer, Women's Health . Many of these center grants from e.g., the National Heart Lung and Blood Institute of the National Institutes of Health, was to establish a multi-disciplinary center for heart and blood vessel disease research (the first in the United States) and the first center to, by design create an integrated, program of basic and clinical research, education and demonstration projects.

With The Methodist Hospital as its primary teaching hospital, Baylor College of Medicine has more than 40 specialty research centers, including centers for Cancer Control Research, Experimental Therapeutics, Gene Therapy, Reproductive Biology, Child Health and Nutrition, Diabetes & Endocrinology, the Human Genome Project and Human Genetics, Developmental Pediatrics, Multi-Organ Transplantation, and Child Health, plus affiliations with 17 other medical institutions and two universities in Houston.

The Methodist Hospital has developed international clinical and training affiliations with hospitals around the world. TMH//BCM bring to the Consortium a world renowned faculty and medical staff with an established commitment to international health care. Facilitated by the activities of the Texas Hadassah Medical Research Foundation, both The Methodist Hospital and Baylor College of Medicine have developed formal ties with the Hadassah Medical Organization, where some work with Chernobyl victims has already begun. In that context, Dr. Shmuel Penchas, Director General of the Hadassah Medical Organization, visited Houston twice during the past year, and ties have been established with organizations involved in resettlement in this country of immigrants from areas affected by Chernobyl. Specific to the proposed research, emigres from the former Soviet Union are on the faculty and will serve as consultants to the proposed projects.

Research Plan and Methods

Figure ____ shows the organizational chart for the proposed research site at TMH/BCM. Armin D. Weinberg, Ph.D., will serve as the Site Director and Principal Investigator and Phillip McCarthy, M.D., will serve as Co-

Principal Investigator. Dr. Weinberg will serve as the representative on the Consortium Steering Committee. In his role as Director of the Center for Cancer Control Research at TMH/BCM, Dr. Weinberg has had ongoing working relations with all the investigators. He is also a trustee of the Texas Hadassah Medical Research Foundation, in which role he co-signed the original letter of agreement to support the collaboration between Russia, Israel and the United States. Dr. McCarthy is head of the Transplant Center at The Methodist Hospital. The principal investigators of the proposed projects will serve together as a research committee to coordinate activities among the studies.

Figure _____

The Methodist Hospital/Baylor College of Medicine

Chernobyl Consortium Research Site - Organization Chart

Site Directors

A.D. Weinberg, Ph.D.

P.L. McCarthy, M.D. Co-principal Investigator

Scientific Advisory Board Research Committee

W.J. Schull, M.D. E. Adam, M.D.

M. Nichaman, M.D. R. Arem, M.D.

A.M. Gotto, Jr., M.D. L.D. Cooley, M.D.

M.E. DeBakey, M.D. A. Ertan, M. D.

P.L. McCarthy, M.D.

Consulting Investigators A. I. Schafer, M.D.

W.J. Schull, M.D. G. Trey, M.P.H., M.D.

M. Nichaman, M.D. A.D. Weinberg, Ph.D.

G. Yoffe, M.D.

E.M. Vainrub, M.D.

The Scientific Advisory Board will provide broad direction for the research as it evolves. The Board will be chaired by William J. Schull, M.D.. He is a population geneticist at the University of Texas School of Public Health and has over 40 years experience working with radiation sequelae in Hiroshima. Milton Nichaman, M.D., is an epidemiologist, also at the University of Texas School of Public Health. He has extensive experience working with the health care system in Israel. Antonio M. Gotto, Jr., M.D., is Chairman of the Department of Medicine at TMH/BCM, and is internationally known as an expert on lipid disorders. Michael E. DeBakey, M.D., is Chairman of the Department of Surgery at TMH/BCM, and is also internationally known for his pioneering work in cardiac surgery.

Working in a more ongoing fashion with the investigators a group of Consulting Investigators. Drs. Schull and Nichaman will also serve on this group. Additional consultation will be provided by Galina Yoffe, M.D., a pediatric hematologist/oncologist and native of the former U.S.S.R. who spent many years in Israel prior to coming to Houston. Elizabet M. Vaintraub, M.D., a pediatrician, will also serve as a consultant. She has immigrated within the past year from Kiev, Ukraine, and has personal knowledge of the Chernobyl accident and its after affects in the contaminated areas. Dr. Vaintraub was with the Ukrainian Ministry of Health and directed their efforts to assess the impact of Chernobyl on the children remaining in the region. Her first hand knowledge of the accident and what followed coupled with her personal relationship with many of the scientist in the former Soviet Union will certainly be an asset as we participate in the consortium's effort to establish a Bryansk research site. Dr. Vaintraub also has indicated a willingness to assist in efforts to bring the Ukraine and Byelorussia into the research efforts spawned by the agreement.

The Research Committee will be composed of the principal investigators of the various TMH/BCM studies. They will meet regularly to coordinate activities among the projects.

Proposals for the pilot research studies are found at the end of this section. The studies and investigators are as follows:

1. U.S. National Chernobyl Registry Coordinating Center (E. Adam, M.D., and A.D. Weinberg, Ph.D.)
2. A Comparative Study of Mental Health Status, Health Beliefs, and Health/Risk Behaviors Among Immigrants from the Area of Chernobyl (A.D. Weinberg, Ph.D.; L. Laufman, Ed.D.; J. Cousins, Ph.D; A. Siegel, Ph.D.)
3. Proposals for Cytogenetic Research (3.1-3.5) (L.D. Cooley, M.D.; P.L. McCarthy, M.D.; A.I. Schafer, M.D.)
4. Proposal to Study Isolated Hematopoietic Stem Cell Populations (P.L. McCarthy, M.D.)
5. Radiation Injury to Vascular Endothelium (A.I. Schafer, M.D.)
6. Epidemiology and Management of Thyroid and Parathyroid Neoplasia and Other Endocrine Abnormalities in Radiation-Exposed Populations (R. Arem, M.D.)
7. Late Radiation Injury of the GI Tract (G. Trey, M.P.H., M.D.; A. Ertan, M.D.)

As a context to the proposed pilot studies, there are several major issues facing the proposed consortium for studying the radiation effects of the Chernobyl accident:

It is important to determine the feasibility of collecting data on the number of people in the Chernobyl region and to quantitate the amount of radiation exposure to dosimetry studies. At TMH/BCM, our concern is that there is no consistently good, reliable biologic or physiologic means of measuring radiation exposure, especially this long after the original event, as noted by Dr. Schull in early conversations. While we agree that it is most important for dosimetry levels to be obtained, reconstruction of the actual dose each person has been exposed to will probably be impossible. Thus the need for historical data and reconstruction of group dose and individual dose must be evaluated.

Given these concerns, we feel that several pilot studies should proceed. The importance of initiating these can provide useful information. For instance, the first two projects regarding a U.S. National Chernobyl Registry and a comparative study of mental health status and health beliefs can be done without dosimetry readings. Indeed, establishment of a registry to locate the potential victims is a necessary first step before the other studies can proceed.

For the cytogenetic proposal (#3), dosimetry studies would be helpful to give us a better idea of who best to screen. However, cytogenetics themselves can be used as a measure of somatic cell mutation and can sometimes be the only means of determining dose rate, depending on the number of people sampled from a particular area.

Proposal #4, to study isolated hematopoietic stem cell populations could be done at all three research sites, in Russia, Israel, and the United States. Our original thinking targeted Briansk so that a leukopheresis machine would be part of the proposal and would be given to the Russians as part of the project for clinical use. We would still use the machine for isolating white blood cells for stem cell isolation and study. This again could be done in any of three research sites. It does not depend on the presence of a registry in that it is also a feasibility study to see how cost-effective this would be.

Proposal #5, to study radiation injury to vascular endothelium, can also be done in all three sites, and again does not require a database for it to take place in that a large number of studies proposed are in vitro work.

For Proposal #6, on thyroid and parathyroid neoplasia, dosimetry obviously would be important, but again this proposal can be done without dosimetry readings. Somatic cell mutation such as thyroid endocrine abnormalities could be done if you were able to screen a large enough population of people and in itself, thyroid abnormality can be a measure of radiation exposure. In fact, it may be as good as any soil sampling or water analysis in that the thyroid is readily accessible.

Proposal #7 is to study late radiation injury of the GI tract and can also be done within the context of a large number of patients. It would not be necessary to have doses of radiation if there is available a good geographic listing of where these patients came from.

On the whole, these studies are the first step in being able to understand the feasibility of whether or not biologic dosimetry would provide an alternative means to actual radiation dosimetry where dose reconstruction takes place on the basis of environmental sampling. Now that the Chernobyl explosion has taken place over six years ago, any physical reconstruction would be most difficult. A significant issue and important concern would be localizing people to a geographic location and trying to reconstruct radiation exposure on the basis of the data that have already been collected within the former Soviet Union. We can then begin comparisons to somatic cell mutation through biologic studies. That is the whole purpose of this type of endeavor and these studies may provide accurate dosimetry readings if any endocrine, GI, hematologic, cytogenetic or endothelial cell abnormalities have occurred, and are able to be quantitated.

A tentative time line for phasing in the projects is found on Exhibit "C".