Health Physics News

Volume XXXII Number 8 For Specialists in Radiation Safety August 2004

The Official Newsletter of the Health Physics Society

In This Issue

Radioactive Iodine Exposure and Thyroid Disease

NCI Chornobyl Health Effects Epidemiological Study

Gen Roessler

What is the dose-response relationship between exposure to ^{131}I from the Chornobyl nuclear reactor accident and thyroid diseases, including cancer and nonmalignant thyroid abnormalities?

This is the major question that the National Cancer Institute (NCI), along with Columbia University and colleagues in Ukraine and Belarus, hopes to answer in its ongoing, long-term epidemiological study of thyroid abnormalities in children who were most at risk of exposure to radioactive iodines from Chornobyl.

Dr. Maureen Hatch, Head of the Chornobyl Research Unit, Radiation Epidemiology Branch at NCI, states that this research, supported by NCI, is significant as a radiation-effects study for a number of reasons:

- It is a population-based, prospective cohort study, involving biennial screening examinations of the thyroid gland with assessment of nonmalignant as well as malignant diseases.

- The individual radiation dose estimates are based on the thyroid activity measurements made close in time to the accident and make use of questionnaire data on residence and diet as well as of models simulating ^{131}I in the environment and in the body.

- Data on factors that may modify the response to radiation, such as age at exposure, gender, or family history of thyroid disease, have been collected carefully and in detail.

- The two parallel arms of the study in Ukraine and Belarus, the countries most contaminated by fallout from the accident, provide the possibility both to compare results and to combine data to increase the precision of estimates (for effect modification, for example) and increase the power to examine rarer forms of thyroid disease.

To put together a comprehensive look at the history of the study and of the methodology used to establish a strong epidemiological conclusion, *Health Physics News* interviewed Dr. Hatch along with Ihor Masnyk, PhD (US Chornobyl Project Director, NCI), Geoffrey Howe, PhD (Principal Investigator for the Columbia University contribution to the study), Mykola Tronko, MD (Project Director,

(continued on page 3)

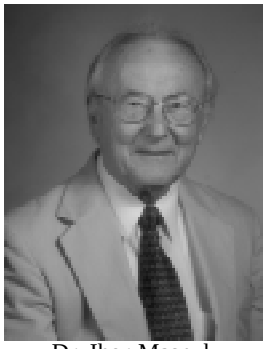
Radioactive Iodine Exposure and Thyroid Disease

(continued from page 1)

Ukraine Thyroid Study), and Eleonora K. Kapitonova, MD (Project Director, Belarus Thyroid Study).

History

The history of this health effects study is long and involved. The US Project Director, Dr. Masnyk, traces the beginnings of interest for a study of this type to August 1986. "After a period of confusion following the accident of 26 April 1986, the Soviet government presented a rather thorough report on the accident and on its efforts to solve the developing problems at an August 1986 International Atomic Energy Agency (IAEA) meeting in Vienna, Austria," he said. "It turns out that Gil Beebe and André Bouville, who would become key persons in the study, were there."



Dr. Ihor Masnyk

"Various international meetings followed and then in 1987 US President Ronald Reagan and Soviet Chairman Mikhail Gorbachev signed an agreement on studies of reactor safety," Masnyk said.

Initial work with the Ukrainians began in 1990 and with the Belarusians later that year. Several years passed in discussions, development of protocols, and funding arrangements. In 1994 and 1995 agreements were reached with Belarus and Ukraine, respectively, for the thyroid studies. Screening examinations started in Belarus in 1997 and in Ukraine in 1998.

"The project in Ukraine, under the leadership of Dr. Mykola Tronko, is operating at a highly satisfactory level and is now in the third cycle of biennial screening examinations," according to Masnyk. "The response rate is maintained at 93% of the original cohort of 13,277 participants. The Belarusian authorities recently moved all of their radiation medicine activities in the newly opened Republican Research Center of Radiation Medicine and Human Ecology (RRCRMHE) in Gomel, Belarus, from the original site of the program in Minsk, Belarus. As a result, work on this part of the project—involving ~12,000 cohort members—was put on hold for more than one year while the transfer was completed. The new director of the Belarusian Thyroid Project is Dr. Eleonora Kapitonova."

Throughout the development of the clinical support for the epidemiological study the dosimetry aspects have been ongoing. Beginning in 1989 Bouville, Ukrainian dosimetrist Professor Ilya Likhtarev, and other dosimetrists have had the responsibility for the estimation of the thyroid doses and of their uncertainties. Details on the dosimetry methods and challenges were summarized in the August 2003 issue of *Health Physics News* in interviews with Bouville, Nickolas Luckyanov, and Paul Voillequé.

The entire team of participants in the study can be found in summary articles on the projects on the NCI Web site at http://dceg.cancer.gov/chornobylThyroidUkraine and http://dceg.cancer.gov/chornobylThyroidBelarus.html.

Study Design and Objectives

There are several studies underway to look at health effects of the Chornobyl accident. However, Hatch emphasizes that "this NCI study is the only **cohort** study of thyroid cancer following the Chornobyl accident. No other study has such a design. Many are case-control studies in which people with and without thyroid cancer are assessed for differences in exposure. Although the case-control approach is a widely used design, it has limitations that the NCI study does not share. For instance, in case-control studies there is a problem of accounting for a screening effect (those exposed to radiation from Chornobyl are more likely to see a physician and come to diagnosis earlier). In our study all subjects are screened, regardless of radiation dose, so there are no differences in ascertainment by exposure status as there might be in a case-control study. The accuracy of our estimates of the excess relative risk will not be biased by a screening effect."

Dr. Maureen Hatch

She added that another significant feature of the NCI study is the range of thyroid disease that the study will be able to evaluate—including endpoints such as hypothyroidism, thyroiditis, and benign nodules whose relationship with radiation is also of interest.

The individual results from each of the two countries, Belarus and Ukraine, according to Hatch, will provide public health information for each country. Scientifically, it will be important to examine the shape of the dose-response curve for each country. If the slopes are similar, this will strengthen interpretation of

the results. It will also be of interest to see whether consistent patterns are seen with modifying factors such as age at exposure. One of the original aims of the study was to combine data from the two arms, after assessing each of them separately. To this end, substantial effort has gone into creating data-collection instruments and data bases that are consistent with one another. Combining the data from the approximately 25,000 cohort members in the two countries will increase statistical power, particularly for the rarer noncancer endpoints.

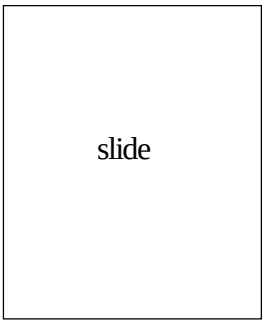
Dosimetry Part of the Study

Since the description of the dosimetry part of the study in the August 2003 *Health Physics News*, the Ukrainian group, under the leadership of Likhtarev, PhD, has continued interviewing cohort members and their parents and is developing a model for dose estimation taking into account ^{137}Cs contamination and iodine prophylaxis. A model of atmospheric transport and deposition of ^{131}I has been developed as well. A recent focus has been on estimating uncertainties in respondents' self-reports using data from several hundred repeat interviews.

Ukraine Thyroid Study

Ukrainian Study Director Tronko has participated in this study since 1993 when he and his country's investigators, together with NCI, wrote the project protocol and the operations manual for project implementation; prepared regulating documents, informed consent forms, warranty of protection of study subjects' rights, and declarations of study subjects' rights; and began recruitment of the study cohort.

"The results of this study will be of much benefit for understanding the impact of radiation exposure on thyroid pathology, most of all thyroid cancer," Tronko said. "Participation in this project is of paramount importance to our country by allowing us to estimate—with a high degree of reliability—the real extent of the aftereffects of the Chornobyl accident on the thyroid status in children and adolescents of Ukraine. In addition, the 13,277 cohort members are given, as needed, timely diagnoses."



Dr. Mykola Tronko

Tronko stated that to date in Ukraine thyroid cancer has been diagnosed in 75 cohort members and benign thyroid pathology has been found in 34 other members. All of them have had surgery and are followed at the Institute of Endocrinology and Metabolism of the Academy of Medical Sciences of Ukraine, Kiev. The incidence of thyroid cancer in children is ordinarily very rare.

Benefits to the Ukrainian investigators, according to Tronko, include being able to study more closely the problem of the epidemiology of thyroid diseases, the dose dependence of thyroid pathology, and issues of radiation carcinogenesis. The investigators also have the opportunity to improve their professional skills, acquire experience with the operation of modern diagnostic equipment, and improve their approaches to the diagnosis and treatment of thyroid disease.

"The main challenge to our investigators is to ensure a high attendance rate of the cohort members at medical screening examinations over the duration of the project," Tronko added.

Belarus Thyroid Study

Belarusian Study Director Kapitonova has been following the project since its beginning through communications with her colleagues in Minsk. Initially she worked at Gomel Medical University and in 1997 started working in the Gomel Branch of the RRCRMHE. Employees of the Branch were already involved in the project as mobile team workers. In 2002 she was appointed as a member of the expert commission of the Belarus Ministry of Health on an evaluation of the project and had to review in detail all of the documents on the project, the operations manual, the group supervisors' reports, and protocols of working meetings.

"In October 2003 when I was appointed as the project director I felt fully confident in the project," Kapitonova said. "The present project methodology is well planned; it is a long-term radiation-epidemiological and scientific research study. All researchers in the project acquire valuable experience during their work in the planning and organization of this kind of study."

"This project," she emphasized, "is of great importance for Belarus from the point of view of the scientific aspects for connecting thyroid diseases with radiation exposures and also from the


Dr. Eleonora Kapitonova

practical side since thyroid diseases are being identified at early stages and then the treatment of the diseases can be provided."

There have been some challenges for the Gomel research team. Kapitonova recalled that during the early stages of project implementation at the RRCRMHE in Gomel the main problem was associated with the resumption of the data coordination activity and the organization of the interaction with the specialists from Minsk who had worked on the study to that date—both problems that have since been solved.

She added that the RRCRMHE Center is a modern diagnostic and scientific clinic where it is possible to provide the high technological types of examinations and treatment for the study cohorts. The clinical framework includes providing fine-needle aspirations of thyroid tissues and immediate diagnoses. Facilities also are available for electronic recording of the ultrasound images of the thyroid and for the image processing and storage.

Kapitonova said benefits to the Belarusian investigators include the scientific contacts and the cooperation of scientists and doctors on all levels. "This information exchange is important for the new institution, the RRCRMHE," she stated. "We are glad to meet new friends and new partners."

Other Related Studies

Hatch mentioned that in addition to the study of thyroid cancer among children in Ukraine and Belarus, a recent addition is a substudy in Ukraine of individuals who were potentially exposed in utero. This is a group for which there is almost no information with respect to radioiodines and thyroid disease. Work is underway to prepare dosimetry algorithms for this substudy.

NCI is also involved in a study of leukemia and other hematologic disorders among clean-up workers in Ukraine. Information about this study, which uses a dose reconstruction method known as RADRUE, can be found at the following URL: http://dceg.cancer.gov/chornobylLeukemiaUkraine.html.

Final Word

"In the end it is the epidemiologist's job to glue together all the pieces of this puzzle and come up with the final word," according to Dr. Geoffrey Howe, Columbia University, a leading epidemiologist in this study. "We take the work of the dosimetrists to develop the dose piece of the study and the work of the clinicians to give us the response piece and then we come up with the risk."


Dr. Geoffrey Howe

"We are often asked if we have enough statistical power in this study to find an association between dose and risk," Howe added. "Power itself is not the main issue here. First of all, what we are doing is based on what is currently known about the risk of **external** radiation. When you do that and apply it to this study we know that we will have more than adequate power. Most important, based on the descriptive studies that have been carried out to date and the thyroid disease epidemic that has been seen in the three countries—Belarus, Ukraine, and Russia—we know there is a radiation effect. What we are trying to do is to quantify that effect as precisely as possible while allowing for possible biasing factors such as screening.

"Therefore, our challenge is to narrow this down to answering the question, 'How big is the risk from internal exposure to ^{131}I?' This is what we need so that we can apply it in the medical field where ^{131}I is used in both diagnostic and treatment situations. Our real objective in this study is to get the most precise estimate of cancer risk to children from internal ^{131}I exposure."

An analysis of the dose-response relationship based on data from the first round of screening in Ukraine will soon be completed. Results will be submitted to a major medical journal. *Health Physics News* will bring an update to its readers on these results as soon as the information is available.

Editor's Note: The study objectives, design, and methodology have recently been published in *Radiation Research*, Vol. 161, No. 4, April 2004:

"A Cohort Study of Thyroid Cancer and Other Thyroid Diseases after the Chornobyl Accident: Objectives, Design and Methods." Chornobyl Thyroid Diseases Study Group of Belarus, Ukraine, and the USA: Valentin A. Stezhko, Elena E. Buglova, Larissa I. Danilova, Valentina M. Drozd, Nikolaj A. Krysenko, Nadia R. Lesnikova, Victor F. Minenko, Vladislav A. Ostapenko, Sergey V. Petrenko, Olga N. Polyanskaya, Valery A. Rzheutski, Mykola D. Tronko, Olga O. Bobylyova, Tetyana I. Bogdanova, Ovsiy V. Ephstein, Iryna A. Kairo, Olexander V. Kostin, Ilya A. Likhtarev, Valentin V. Markov, Valery A. Oliynik, Viktor M. Shpak, Valeriy P. Tereshchenko, Galina A. Zamotayeva, Gilbert W. Beebe, André C. Bouville, Aaron B. Brill, John D. Burch, Daniel J. Fink, Ellen Greenebaum, Geoffrey R. Howe, Nickolas K. Luckyanov, Ihor J. Masnyk, Robert J. McConnell, Jacob Robbins, Terry L. Thomas, Paul G. Voillequé, and Lydia B. Zablotska.