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MEETING REPORT

Research Symposium on Radiation and Cancer Honors Dr. Elaine Ron

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On March 9, 2011, NCI's Division of Cancer Epidemiology and Genetics (DCEG) held a memorial symposium on Research Strategies in Radiation and Cancer to honor Dr. Elaine Ron, a senior investigator in DCEG and a widely respected expert in the field of radiation epidemiology. Dr. Ron died of cancer on November 20, 2010 (see In Memoriam: Elaine Ron; http://dx.doi.org/10.1667/RRXX36).

Dr. Joseph F. Fraumeni, Jr., director of DCEG, provided opening remarks. ''Elaine was an enormously gifted epidemiologist whose groundbreaking research has contributed greatly to a better understanding of the risks of cancer associated with a wide variety of exposures to ionizing radiation,'' said Dr. Fraumeni. ''As a tribute to Elaine, it seemed fitting to assemble an elite group of Elaine's collaborators and peers to reflect on the significance of her contributions to radiation epidemiology and to explore strategies that are likely to accelerate progress in the field.''

Six internationally renowned researchers studying diverse aspects of radiation exposure and cancer risk discussed seminal studies that Dr. Ron either had led or in which she collaborated. Former and current DCEG research fellows from Israel, Russia, the Netherlands, Brazil and the United States also spoke about the dedicated mentoring Dr. Ron provided throughout her career, which has influenced a new generation of radiation epidemiologists. To underscore Dr. Ron's commitment to interdisciplinary research and to radiation epidemiology projects with important public health and clinical application, the Director of the International Agency for Research on Cancer, Dr. Christopher Wild, spoke about two-way translational research from basic science to both clinic and the population. Finally, a panel of DCEG junior investigators delivered presentations in a panel discussion on ''Evolving Research Strategies in Radiation'' (http://dx.doi/10.1667/RRXX37.1), which highlighted new tools and new areas of study for radiation epidemiologists to consider as the field evolves.

The session entitled ''Successful Strategies in Radiation'' featured six leading researchers who presented scientific highlights of studies that focused on acute and protracted low- and high-dose radiation exposures reflecting Dr. Ron's wide-ranging research interests. The speakers highlighted successful research strategies that Dr. Ron had initiated in those studies. The common themes echoed in those presentations were Dr. Ron's passion to do the best science possible; her strategic vision in asking and answering important questions; her ability to identify populations in which critical gaps in understanding of radiation-related risks could be fruitfully addressed; her rigor in study design and implementation; and her deep commitment to training the next generation of investigators.

Dr. Charles Land summarized the history of the Radiation Effects Research Foundation and the contribution of Dr. Ron to two major reports of cancer incidence in survivors of the atomic bombings in Japan. The first report was a landmark four-part series that used data from population-based tumor registries in Hiroshima and Nagasaki in the first incidence studies in the survivors that focused on risks of solid tumors, risks of leukemia, lymphoma and multiple myeloma, and a comparison of cancer incidence and mortality (*1–4*). Dr. Ron also coauthored the second incidence report with updated risk estimates from an additional 10 years of follow-up (*5*). Dr. Ron also played a central role in site-specific studies of skin cancer (*6*), brain and central nervous system tumors (*7*), male breast cancer (*8*) and papillary thyroid microcarcinoma (*9*).

Dr. Dale Preston presented highlights from the studies in the Russian Federation that are investigating the relationship between cancer mortality and protracted radiation exposure from the Mayak nuclear facility in Ozyorsk, Russia to workers and from radioactive waste from the facility to the population living in proximity. The study focuses on 26,000 nuclear workers and 30,000 villagers living near the Techa River, which was polluted with highly radioactive waste from 1949 to the mid-1950s. Recent results revealed dose-related increases in solid cancer and leukemia among Mayak workers who were chronically exposed to external radiation and increased risks of cancers of the lung, liver and bone among workers exposed to plutonium (*10*). Elevated risks of solid cancer, breast cancer

and leukemias were observed among exposed Techa River villagers (*11–13*). Dr. Ron and collaborators also launched a study of cancer incidence and mortality among persons exposed *in utero* while their mothers worked at the Mayak facility.

Dr. Shirley Fry described findings from studies that evaluated the increased risk of thyroid cancer in children (*14, 15*) and leukemia in clean-up workers (*16*) after the Chernobyl nuclear disaster. Dr. Ron served for many years on the oversight committee for the NCI-Columbia University study of cancer and other late effects from the Chernobyl accident. The most recent Chernobyl study indicated that the risk of thyroid cancer continues for 20 years and later in children who were exposed to ^{131}I after the accident (*14*).

Dr. Arthur Schneider discussed the pooled analysis of thyroid cancer after exposure to external radiation that remains a major source of radiation risk estimation for thyroid cancer (*17*). Dr. Ron and colleagues pooled data from seven studies to provide detailed information characterizing dose-related radiation risks and establish that thyroid cancer risk is highest for children and continues up to 40 years after exposure. An expansion of a pooled analysis is under way that includes the original investigations and six additional studies.

The etiology of thyroid cancer related to non-radiation risk factors was also investigated in the original pooled analysis of thyroid cancer case-control studies (*18*). Dr. Silvia Franceschi provided highlights from the pooled study that suggested an increased risk of thyroid cancer associated with goiter and benign nodules/adenomas and to a lesser extent with reproductive factors (mostly among women who developed thyroid cancer at young ages) and with height and weight (although there was heterogeneity among the studies).

Recognizing the importance of children's enhanced sensitivity to radiation compared to adults and the increasingly widespread use of CT scans in children, Dr. David Brenner reviewed the current data on projections of cancer due to CT use in children (*19, 20*). In response to this growing concern about CT use, Dr. Ron and colleagues initiated a cohort investigation that is currently evaluating cancer risk after childhood exposure to CT scans in the United Kingdom. The findings from this cohort study will inform which specific cancers in the population should be evaluated with more detailed dosimetry in case-control studies.

After these presentations, there was a panel discussion by the six investigators that identified the important research issues that need to be addressed in radiation epidemiology. The major issue is the effect of low-dose and low-dose-rate radiation on cancer risks and biological markers of risk. A second key gap is the need to identify of radiation-sensitive population subgroups and to determine the reasons for the heterogeneity of radiation-related risk in populations. To evaluate this heterogeneity, what is required is improvement in the accuracy of dose estimates, calculation of the uncertainties associated with these estimates, and evaluation of how uncertainties in dose affect risk estimates. A third area requiring additional research is the need to quantify site-specific organ risks and to evaluate the interaction of radiation with other factors to better understand the biology of radiation carcinogenesis. Pooling of epidemiological studies will likely be required to achieve sufficient statistical power to address these site-specific risks. A fourth topic is the importance of understanding the molecular signatures of ionizing radiation particles, which will likely be more successful for high- than low-linear energy transfer (LET) radiation. Finally, the panel concluded that the development of appropriate translation of findings from epidemiological and radiobiology studies to clinical practice will be a challenge but can be informed by such studies.

APPENDIX

The ABCs of Lessons Learned from Dr. Elaine Ron

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- A true leader identifies and focuses on important research questions that are scientifically interesting, relevant for public health, and feasible in time and budget constraints.
- Ask difficult questions of yourself and your colleagues about all aspects of the research.
- Avoid working on too many projects at the same time.
- Be creative and persistent to succeed with your projects.
- Be realistic in assessing your time and ability to accomplish tasks.
- Create and maintain good professional networks.
- Define your goals clearly.
- Fight for what you believe in.
- Good humor is essential.
- Follow your heart to select projects that truly excite you.
- Keep the fundamental epidemiologic principles in mind—no matter how complicated/sophisticated the study or analysis.
- Listen.
- Medical scientists should always be thinking about those who are the reason for our work, the patients.
- Support your colleagues and in particular, nurture young scientists to help them reach their maximum potential.
- Take notes in pencil.
- There is more to life than just research.
- Think outside of the box.

- To be a successful investigator, it takes not only an excellent scientist, but first and foremost, an efficient manager and a talented research leader.
- You achieve scientific progress with good questions and good questions need excellent answers.

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