The National Academies of
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GILBERT W. BEEBE SYMPOSIUM ON 30 YEARS AFTER THE CHERNOBYL ACCIDENT

CURRENT AND FUTURE STUDIES ON RADIATION HEALTH EFFECTS

November 1-2, 2016

Auditorium
National Academy of Sciences Historic Building
2101 Constitution Ave NW, Washington, DC 20418

The symposium is hosted by the Nuclear and Radiation Studies Board of the National Academies and co-sponsored by the National Cancer Institute, the Environmental Protection Agency, and the National Institute of Allergy and Infectious Diseases.

AGENDA

DAY 1: November 1, 2016

8:30 AM	**Call to order and welcome (5')** *Jonathan M. Samet, University of Southern California*

PLENARY SESSION
Moderated by Jonathan M. Samet, University of Southern California

8:35 AM	**Gilbert W. Beebe's Contributions in Radiation Research (10')** *John D. Boice, National Council on Radiation Protection and Measurements*
8:50 AM	**Overview of the Chernobyl Accident (25')** *Mikhail Balonov, Institute of Radiation Hygiene, Russia*
9:20 AM	**Doses Received from the Chernobyl Accident (15')** *Andre Bouville, National Cancer Institute (retired)*
9:40 AM	**Dosimetry during the Chernobyl Accident (20')** *Vadim Chumak, National Academy of Medical Sciences of Ukraine*
10:00 AM	**Medical Aftermath of Chernobyl Accident in the Republic of Belarus (15')** *Ilya Veyalkin, The Republican Research Centre for Radiation Medicine and Human Ecology, Belarus*
10:20 AM	**BREAK**

SESSION 1: Immediate and Late Health Effects in First Responders
Moderated by Scott Davis, University of Washington

10:35 AM	**Immediate Health Effects (15')** *Fred A. Mettler Jr., University of New Mexico School of Medicine (Professor Emeritus)*
10:55 AM	**Late Health Effects (25')** *Dimitry Bazyka, Academy of Medical Sciences of Ukraine*
11:25 AM	**Questions and Discussion for Session 1 with Audience Participation**
11:50 AM	**LUNCH (Available for purchase at the refectory—lower level)**

SESSION 2: Late Cancer-Related Health Effects in the General Population

Moderated by Scott Davis, University of Washington and Mykola Tronko, Ukraine-U.S. Thyroid Project, Kiev, Ukraine

1:00 PM	**Thyroid Cancer (25')** *Ausrele Kesminiene, International Agency for Research on Cancer*
1:25 PM	**Leukemia and Breast Cancer (20')** *Lydia B. Zablotska, University of California, San Francisco*
1:45 PM	**Questions and Discussion for Session 2 with Audience Participation**

SESSION 3: Other Health Effects

Moderated by Lawrence T. Dauer, Memorial Sloan Kettering

2:10 PM	**Cataracts (20')** *Norman J. Kleiman, Columbia University*
2:35 PM	**Cardiovascular Health Effects (15')** *Kiyo Mabuchi, National Cancer Institute*
2:50 PM	**Health Effects of *In Utero* Exposure (15')** *Maureen Hatch, National Cancer Institute*
3:10 PM	**Questions and Discussion for Session 3 with Audience Participation**
3:30 PM	**BREAK**

SESSION 4: Psychosocial Effects and Community Resilience

Moderated by Merriline M. Satyamitra, National Institute of Allergy and Infectious Diseases

3:50 PM	**Experience from Chernobyl (20')** *Evelyn J. Bromet, Stony Brook University School of Medicine*
4:15 PM	**Lessons Learned from other Disasters (20')** *Dean G. Kilpatrick, Medical University of South Carolina*
4:40 PM	**Advances in Community Resilience Research (20')** *Benjamin Springgate, Louisiana State University Health New Orleans*
5:00 PM	**Questions and Discussion for Session 4 with Audience Participation**
5:30 PM	**Closing Remarks, Adjourn Day 1** *Merriline M. Satyamitra, National Institute of Allergy and Infectious Diseases*

DAY 2: November 2, 2016

8:30 AM	**Call to Order and Welcome (5')** *Jonathan M. Samet, University of Southern California*

SESSION 5: Advances in Radiation Research
Moderated by Mikhail Frydman, Republic Centre for Thyroid Tumors, Minsk, Belarus and Fred A. Mettler Jr., University of New Mexico School of Medicine (Professor Emeritus)

8:35 AM	**Biodosimetry (15')** *Lynne K. Wathen, Biomedical Advanced Research and Development Authority*
8:55 AM	**Medical Countermeasures (15')** *David R. Cassatt, National Institute of Allergy and Infectious Diseases*
9:10 AM	***–Omics* (15')** *Stephen J. Chanock, National Cancer Institute*
9:30 AM	**Genetic Markers (15')** *Yuri E. Nikiforov, University of Pittsburgh Medical Center*
9:50 AM	**Tissue Banking (15')** *Geraldine Thomas, Imperial College, London, UK*
10:05 AM	**Questions and Discussion for Session 5 with Audience Participation**
10:40 AM	**BREAK**
11:00 AM	**Research on the Aftermath of Chernobyl: Have Lessons been Learned? (20')** *Jonathan M. Samet, University of Southern California*
11:25 AM	**General Discussion and Comments** *Moderated by Lawrence T. Dauer, Memorial Sloan Kettering*
12:00 PM	**Closing Remarks, Adjourn Symposium** *Jonathan M. Samet, University of Southern California*

SESSION ABSTRACTS

PLENARY SESSION

Gilbert W. Beebe's Contributions in Radiation Research

John D. Boice, Jr., National Council on Radiation Protection and Measurements

This presenter will discuss the scientific achievements of Gilbert W. Beebe with emphasis on Chernobyl studies. He will also share his own experience with working with Dr. Beebe at the National Cancer Institute in what would become the Division of Cancer Epidemiology and Genetics.

Overview of the Chernobyl Accident

Mikhail Balonov, Institute of Radiation Hygiene, Russia

The Chernobyl accident had by far the largest radiological consequences from all the radionuclide releases to the environment. In 1986, the USSR authorities has undertaken enormous efforts for accident mitigation. Simultaneously, large scale protective actions started for protection of the public. In some areas of Europe, primarily in Belarus, Russia and Ukraine, remedial actions are still in progress.

On the accident day, more than 500 emergency workers received large radiation doses that resulted in 134 ARS cases among them. In 1986-1990, more than 500 thousand recovery operation workers were exposed to elevated radiation doses. The corresponding health effects are under scrutiny. More than five million people live in areas of Belarus, Russia and Ukraine with elevated radiation levels. The most radiologically significant exposure pathway for them was internal exposure to radioiodine in food in April-May 1986. That pathway resulted in high thyroid doses and, later on, in development of several thousand thyroid cancer cases in children (as of 1986). Further long-term external and internal exposure of the public to radiation of Cs radionuclides did not result in discernible health effects.

The Chernobyl accident opened wide opportunities for radiological research. Over the last 30 years,

- Some new low dose health effects revealed (e.g., thyroid cancer from radioiodine, cataract),
- Knowledge of radiation-induced health effects advanced from worker and public studies,
- Infrastructure for further epidemiological and radiobiological studies created.

Ample research opportunities are still open, many promising studies go on.

Doses Received from the Chernobyl Accident

Andre Bouville, National Cancer Institute (retired)

The explosions at the Chernobyl nuclear power plant in Ukraine early in the morning of April 26, 1986 led to radiation exposures of large numbers of workers and of members of the general public. The presentation is an overview of the doses received by: (1) the approximately 500,000 clean-up workers who came to the Chernobyl site between 1986 and 1990, (2) the 116,000 people who were evacuated from areas surrounding the reactor during 1986, (3) the 5 million people who resided in the contaminated areas of Belarus, the Russian Federation, and Ukraine, and (4) the 500 million people from other European countries. The doses resulting from the Chernobyl accident are also compared to those from the Fukushima accident, which occurred in Japan on March 11, 2011.

Dosimetry during the Chernobyl Accident
Vadim Chumak, National Academy of Medical Sciences of Ukraine

In many respects the Chernobyl accident is the largest nuclear accident ever: the magnitude of radioactive release, the scale of radioactive contamination of the environment and the number of persons involved into the accident (both public and professionals) are unparalleled. The main cohorts affected by the accidental exposure are: clean-up workers (so-called 'liquidators'), evacuees from the nearby areas (the 30-km zone) and general population of contaminated territories. The impact (individual and collective doses), exposure pathways and practical approaches to quantification of their doses are very different. If dosimetry of these cohorts is concerned, one should distinguish direct dose measurements (individual monitoring), measurements of body burden (thyroid and whole body) and other relevant measurements (i.e. dose rates) taken at the time of the accident to assist further dose assessment/reconstruction, which involved various kinds of modeling. The presentation is devoted to discussion of all three aspects of dosimetry at the time of the Chernobyl accident (1986-1990). Summarizing review of dosimetry in Chernobyl, one should keep in mind that aforesaid data is essential, but not sufficient – in order to obtain individual or group dose estimates, dosimetric models should be employed, engaging other data inputs (i.e. behavior or intake profiles) or assumptions.

Medical Aftermath of Chernobyl Accident in the Republic of Belarus (15')
Ilya Veyalkin, The Republican Research Centre for Radiation Medicine and Human Ecology, Belarus

The speaker will characterize the demographic situation in different groups of people affected by the Chernobyl disaster. He will also describe incidence and mortality rates and structure in these cohorts. Much attention will be paid to cancer incidence rates in Belarus before and after Chernobyl disaster. Especially standardized cancer incidence ratios will be described for affected people versus Belorussian population. Thyroid cancer and leukemia in suffered people will be presented in detail.

SESSION 1: Immediate and Late Health Effects in First Responders

Immediate Health Effects
Fred A. Mettler Jr., University of New Mexico School of Medicine (Professor Emeritus)

The Chernobyl accident resulted in almost one-third of the reported cases of acute radiation sickness reported worldwide. Cases occurred among the plant employees and first responders but not among the evacuated populations or general population. The diagnosis of acute radiation sickness was initially entertained for 237 persons based on symptoms of nausea, vomiting and diarrhea. Ultimately, the diagnosis of ARS was confirmed in 134 persons. There were 28 short term deaths of which 95% occurred at whole body doses in excess of 6.5 Gy. Underlying bone marrow failure was the main contributor to all deaths during the first 2 months.

Allogenic bone marrow transplantation was performed on 13 patients and an additional 6 received human fetal liver cells. All of these died except one individual who later was discovered to have recovered his own marrow and rejected the transplant. Two or three patients were felt to have died as a result of transplant complications. Skin doses exceeded bone marrow doses by a factor of 10-30 and at least 19 of the deaths were felt to be primarily due to infection from large area beta burns. Internal contamination was of relatively minor importance in treatment. By the end of 2001 an additional 14 ARS survivors died from various causes. Long term treatment has included therapy for beta burn fibrosis and skin atrophy as well as for cataracts. There apparently has been no comprehensive follow-up of this group of patients since 2007.

Late Health Effects

Dimitry Bazyka, Academy of Medical Sciences of Ukraine

Studies of health effects of Chornobyl in a group of NPP employees and first responders with acute radiation syndrome were started in April 1986. On stochastic effects the main findings after the 2008 UNSCEAR report were obtained in joint studies by the RCRM and the U.S. NCI. A case-control study in a cohort of 100,645 cleanup workers exposed at low dose and low dose rates demonstrated increased radiation risks comparable with hibakusha data (ERR/Gy for first 15 years – 3.44; 95% CI: 0.47; 9.78; p<0,01; ERR/Gy for 20 years – 2.38; 95% CI 0.49; 5.87; p<0.004). At the 2016 RCRM study an increased chronic lymphocytic leukemia incidence was revealed for 26 years (1987-2012) after the exposure (SIR 1.44 (95% CI: 1.21; 1.68). The RCRM-NCI-Columbia University-UCSF study provided new evidence on the association of radiation dose and younger age at first radiation exposure at Chornobyl with shorter survival after diagnosis.

Several studies are performed in an updated cohort of 152,520 male cleanup workers 22–26 years after exposure and a significant excess was registered in incidence of multiple myeloma (SIR 1.61, 95% CI 1.01; 2.21) and thyroid cancer (TC) (SIR 3.50, 95% CI 3.04; 4.03). In a parallel RCRM study risks were demonstrated for all solid cancers (SIR 1.08; 95% CI 1.05; 1.11) and TC in evacuees exposed to radioiodine (SIR for 1990–2012: 401.8; 95% CI: 359.2–449.3).For some effects there is no consensus on radiation origin due to high prevalence in unexposed population (cardio- and cerebrovascular diseases, mental health changes) and difficulties in reconstructive dosimetry. Analytical cohort and case-control studies are in need on circulation pathology, late high dose effects, specific types of radiogenic cancers, second cancers after leukemia using molecular epidemiology approach.

SESSION 2: Late Cancer-Related Health Effects in the General Population

Thyroid Cancer

Ausrele Kesminiene, International Agency for Research on Cancer

Studies of the extensive thyroid gland exposure sustained as a result of the Chernobyl accident, particularly in childhood, produced a new bulk of evidence of the radiosensitivity of paediatric thyroid gland to exposure from internally incorporated radioactive iodine isotopes. Thirty decades after the accident, the increased risk of thyroid cancer is still observed in those exposed, although pattern of the risk in longer term remains to be confirmed. An impact of various host and environmental factors on the risk of radiation induced post-Chernobyl thyroid cancer, has been postulated but the clear picture needs to be obtained.

Leukemia and Breast Cancer

Lydia B. Zablotska, University of California, San Francisco

We recently passed the somber 30-year mark of the worst nuclear power plant accident known to mankind. In the aftermath of the 1986 Chernobyl nuclear power plant accident in Ukraine, general population from the areas around the plant was exposed to various types and doses of ionizing radiation. With bone marrow being one of the most radiosensitive tissues in the body, there was a great interest in studying risks of leukemia in children and adults from this population. In this presentation we will summarize published reports describing leukemia prevalence and incidence in the populations living in the radiation-contaminated areas of Ukraine, Belarus and Russia and further afield in Europe. Because the majority of these reports were descriptive in nature, currently there is no reliable scientific evidence on the effects of Chernobyl exposures on the risks of leukemia in the general population after the Chernobyl accident.[1] Epidemiological studies of cleanup workers from Ukraine,[2,3] Belarus, Russia and Baltic countries,[4] and registry-based studies from Russia[5] reported significantly increased radiation risks of leukemia. The study of Ukrainian cleanup workers raised an intriguing possibility that radiation exposures could increase the risks of all types of leukemia, including chronic lymphocytic leukemia (CLL), heretofore considered not radiation-related.[3] Whether the increased radiation risks of CLL are due to the Chernobyl-related radiation exposures, other environmental exposures or to some specific characteristics of CLL in the Ukrainian population is unknown. We will present the results of recent genetic and genomic studies of CLL in paired samples from cleanup workers, general population from Ukraine and the U.S. aimed at clarifying the nature of these risks. Further epidemiological studies are necessary to understand the nature and magnitude of these risks and whether they could be explained by genetic and genomic changes induced by radiation exposures.

1. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 2008 Report to the General Assembly with Scientific Annexes. Volume II. Annex D: Health Effects Due to Radiation from the Chernobyl Accident. New York: United Nations; 2011.
2. Romanenko A, Finch S, Hatch M, et al. The Ukrainian-American study of leukemia and related disorders among Chornobyl cleanup workers from Ukraine: III. Radiation risks. *Radiat Res*. 2008;170(6):711-720.
3. Zablotska LB, Bazyka D, Lubin JH, et al. Radiation and the risk of chronic lymphocytic and other leukemias among chornobyl cleanup workers. *Environ Health Perspect*. 2013;121(1):59-65.
4. Kesminiene A, Evrard AS, Ivanov VK, et al. Risk of hematological malignancies among Chernobyl liquidators. *Radiat Res*. 2008;170(6):721-735.
5. Ivanov VK, Tsyb AF, Khait SE, et al. Leukemia incidence in the Russian cohort of Chernobyl emergency workers. *Radiat Environ Biophys*. 2012;51(2):143-149.

SESSION 3: Other Health Effects

Cataracts
Norman J. Kleiman, Columbia University

The lens of the eye is one of the most radiosensitive tissues in the human body. Nevertheless, until recently, human ocular radiation exposure guidelines were based on the assumption that the primary ocular pathology associated with low-dose radiation exposure, radiation cataract, was a deterministic event requiring threshold doses of 2 Gy or greater. In part, this assumption was based on older studies which generally had short follow-up periods, failed to take into account increasing latency as dose decreased, had relatively few subjects with doses below a few Gy and were not sensitive enough to detect early radiation-associated lens changes. Newer findings in populations exposed to much lower radiation doses, including the Chernobyl Liquidator cohort, strongly suggest dose-related lens opacification at significantly lower doses. Experimental animal studies, as well as dilated slit lamp eye examinations of mice and voles living in the Chernobyl exclusion zone, support these findings. Other animal studies suggest that specific genetic determinants influence radiation cataract risk. These newer data have led to a recent re-evaluation of previous lens occupational exposure guidelines and a recommended lowering of the presumptive radiation cataract threshold regardless of whether exposure was acute, protracted or chronic. The new guidelines are likely to have significant implications for future occupational exposure and the need for eye protection in interventional medicine, and have influenced current research efforts concerning the cellular and molecular mechanisms underlying radiation cataractogenesis.

Cardiovascular Health Effects
Kiyo Mabuchi, *National Cancer Institute*

Cardiovascular disease effects of low-dose radiation have been debated since evidence of increased risk of non-cancer disease mortality, mostly from cardiovascular disease, emerged from the Life Span Study cohort of Japanese atomic-bomb survivors in late 1990s. Cardiovascular disease risk associated with low-dose radiation exposure is an important public health concern. This is because relative risks associated with radiation exposure appear smaller, compared with cancer, but the absolute risk could be large because of high baseline cardiovascular disease rates in many adult populations. The Chernobyl accident resulted in massive radiation exposure, involving a large number of populations exposed in various manners, providing important opportunities for learning about the radiation-related risk of low dose and dose-rate exposure, as contrasted from acute exposure from the atomic bombs, on cardiovascular disease.

The most recent 2008 UNSCEAR Report reviewed epidemiological data on cardiovascular disease effects. Most notable was a significant dose response found for various endpoints of cardiovascular disease in the Russian recovery workers, with the estimated excess relative risk comparable to that found in the atomic-bomb survivors. Cardiovascular data in the Russian recovery worker cohort, the Ukrainian State Registry and Belarusian regional mortality patterns have all been updated. However, a major limitation with Chernobyl studies, and for that matter, with many other studies, continues to be failure to exclude the possibility of lifestyle and other factors confounding the apparent association between radiation exposure and cardiovascular disease. The difficulty in estimating doses many years after the accident is another limitation. Nevertheless, the Chernobyl populations, with their large size and relatively high levels of exposure, are a valuable resource for risk assessment and possibly mechanistic studies, and a few ideas for future direction will be offered.

Health Effects of *In Utero* Exposure

Maureen Hatch, National Cancer Institute

Since 2002, the US National Cancer Institute (NCI) and the Institute of Endocrinology and Metabolism (IEM) in Kiev, Ukraine have been following a cohort of 2,582 mother-child pairs exposed to radiation from Chernobyl during pregnancy. This presentation will focus on offspring outcomes of *in utero* exposure, for cancer and non-cancer endpoints, reviewing published results and presenting new data.

Chernobyl accident releases were primarily radioiodines, in particular Iodine-131 (I-131) which concentrates in the thyroid gland. Estimates of fetal thyroid I-131 dose derived from maternal doses were developed for all cohort members. The initial research on radiation-related thyroid cancer found striking but non-significant increases based on a small number of cases detected during a screening examination in adolescence. Updated results will be presented based on a second screening and an additional 10 years of follow-up. Associations of dose with all thyroid nodules, both benign and malignant, will also be reported.

Since thyroid function may govern growth, our most recent research on the prenatally exposed cohort has examined radiation dose in relation to anthropometry- both size deviations at birth and measures of growth in adolescence. The full range of outcomes of the cohort pregnancies has also been examined. The presentation will report the results of these recent studies, including a finding linking fetal I-131 dose to a decrease in head circumference.

Session 4: Psychosocial Effects and Community Resilience

Experience from Chernobyl

Evelyn J. Bromet, Stony Brook University School of Medicine

Mental health research after the Chernobyl disaster found increased acute and chronic distress, depression, anxiety, post-traumatic stress, and medically unexplained somatic symptoms compared to non-exposed controls. Consistent with studies after Three Mile Island and Fukushima, evacuees, pregnant women, mothers of young children, and clean-up workers were identified as high risk groups. Findings on the emotional well-being of exposed children were inconsistent. In all studies, perceived exposure was the major risk factor for mental ill health. The Chernobyl Forum, like the President’s Commission on Three Mile Island (TMI) before it, concluded that mental health was the biggest public health problem caused by the accident. Fifty years of research has shown that poor mental health is associated with physical morbidity, disability, and mortality in disaster-affected and non-disaster populations. Yet the TMI and the Forum’s conclusions did not result in the integration of mental health screening into ongoing health monitoring activities. Nor did these conclusions lead to follow-up research on the long-term health and psychosocial impacts of Chernobyl-related mental ill health, education of primary care physicians about the recognition and treatment of common mental disorder among patients with real or perceived radiation exposure, or the implementation of novel interventions to prevent secondary health effects of the mental ill health that occurred in the first two decades. Lastly, the studies conducted in the first two decades did not focus on resilience. Future studies of unbiased samples are needed to complete the long-term picture by including measures of resilience and age-specific mental, cognitive, and physical health outcomes, with an eye toward intervention and prevention.

Lessons Learned from other Disasters
Dean G. Kilpatrick, Medical University of South Carolina

A considerable body of epidemiological research has been conducted documenting the mental health impact of exposure to natural disasters and other mass casualty incidents. The goals of this presentation are to : 1) review major mental health impacts of disaster exposure; 2) describe key factors that influence risk and resilience for disaster-related mental health problems; and 3) suggest ways to apply what has been learned from this research to improve disaster-related mental health prevention, intervention, and planning. The presentation will also address unique aspects of disasters involving possible exposure to radiation or toxic substances that complicates mental health disaster response.

Advances in Community Resilience Research
Benjamin Springgate, Louisiana State University Health New Orleans

Communities' preparedness, response, and recovery from natural or technological disasters may depend in substantial part on the resilience of the community and affected populations. This presentation will highlight models and recent research in community resilience, with emphasis on identifying practical applications of models to enhance community resilience.

SESSION 5: Advances in Radiation Research

Biodosimetry
Lynne K. Wathen, Biomedical Advanced Research and Development Authority

In all potential radiation disasters, the population is likely to encounter a number of complex radiation exposure scenarios, including different dose ranges and dose rates. Therefore, triage and definitive radiation biodosimetry will require multiple tests to measure absorbed dose. Qualitative point-of-care tests are designed to be administered quickly to determine whether an individual has absorbed a minimum threshold radiation dose and needs further medical care. Quantitative high-throughput laboratory-based test that estimate the actual absorbed dose a person has received are also in late-stage development. These quantitative results will be used in conjunction with signs, symptoms, and hematology to give health care providers additional information to treat patients effectively. Five promising biodosimetry tests are currently funded by U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response (ASPR) to identify the most relevant proteomic, genomic and cytologic radiation biomarkers and validate their utility in animal models and humans. Algorithms have been developed to integrate multiple individual biomarker results into a single test result. The two point of care tests in development use different technologies. One is a multiplex lateral-flow immunoassay test and the other is a multi-array cartridge-based electrochemiluminescent test. Both technologies use capillary (fingerstick) blood samples to detect protein biomarkers that increase following gamma or x-ray exposure. Two of the high-throughput tests under development use changes in gene expression patterns to determine the extent of radiation damage from whole blood drawn into specialized collection and stabilization blood tubes. The third high-throughput test advancing toward a product measures chromosomal damage and micronucleus generation to predict absorbed dose. ASPR's Biomedical Advanced Research and Development Authority (BARDA) working with federal and industry partners will enable the development and acquisition of radiation biodosimeters. The Biodosimetry Program's continued success will help the United States prepare for and respond effectively to a radiological incident or nuclear accident.

Medical Countermeasures
David R. Cassatt, National Institute of Allergy and Infectious Diseases

Given the threat of a terrorist attack or accidental exposure to ionizing radiation, the U. S. Federal Government has taken on the task of developing medical countermeasures (MCMs) to treat injuries resulting from a radiological or nuclear incident. Over the last decade, MCM research and development has been funded by agencies within the Department of Health and Human Services as well as the Department of Defense: for early stage studies, the Radiation and Nuclear Countermeasures Program (RNCP) within the NIAID, NIH; and for late-stage development, the Biomedical Advanced Research and Development Authority (BARDA). Since it is anticipated that approval will be via the U. S. Food and Drug Administration (FDA) Animal Rule, these programs have also advanced the development of animal models for hematopoietic, gastrointestinal and lung radiation injuries. By studying the health effects that resulted from human radiation exposures from atomic weapons, such as survivor populations in Hiroshima and Nagasaki, as well as radiological accidents, such the 1986 Chernobyl accident, investigators have gained an understanding of the natural history of radiation exposure in man, and linked this information to the natural history of radiation injury in animals. Furthermore, researchers have learned the importance of early intervention and timely medical management for treatment of patients. A number of products have advanced through various stages of development, with two products (Neupogen® and Neulasta®) being approved to improve survival in people exposed to lethal doses of ionizing radiation; however, these approvals would not have been possible without an understanding of the human radiation experience.

–Omics
Stephen J. Chanock, National Cancer Institute

Abstract not submitted.

Genetic Markers
Yuri E. Nikiforov, University of Pittsburgh Medical Center

Since the early 1990s, when the first cases of thyroid cancer in children exposed to radiation after the Chernobyl accident were registered, a large body of knowledge has been accumulated on genetic alterations and molecular mechanisms of thyroid carcinogenesis associated with exposure to ionizing radiation. Multiple studies of thyroid cancers in post-Chernobyl children and young adults have shown that chromosomal rearrangements leading to gene fusions represent a common genetic mechanism of radiation-associated thyroid cancer. A prototypic example of such chromosomal rearrangements is *RET/PTC*, seen in 30-80% of post-Chernobyl cancers. More recently, another rearrangement, ETV6/NTRK3 has been found to be common and detectable in ~15% of these tumors. These rearrangements appear to be associated with I-131 dose received after Chernobyl and can be induced in cultured human thyroid cells exposed to various types of ionizing radiation. More recent data demonstrate a strong correlation between gene fusions and radiation dose in post-Chernobyl cancer, providing further evidence for the link between chromosomal rearrangements and radiation exposure. It has also been shown that genes participating in RET/PTC rearrangements are located close to each other in the nuclei of normal thyroid cells, providing structural basis for mis-joining free DNA ends located in proximity to each other. However, it remains unknown if such oncogenic chromosomal rearrangements are formed as a direct result of double-strand DNA breaks induced by exposure to radiation or indirectly and via what mechanism of DNA repair.

Tissue Banking
Geraldine Thomas, Imperial College, London, UK

The Chernobyl accident in 1986 gave scientists around the world the opportunity to study what is normally a very rare type of cancer – thyroid cancer in young children and adolescents – and the opportunity to link environmental exposure of a carcinogen (in this case, radiation) to the molecular and clinical phenotype of the disease. However, access to human samples is seldom easy, particularly when the samples come from young people in a different country. The Chernobyl Tissue Bank (CTB) was established in 1998 to ensure that there was co-ordination of these studies and to provide infrastructure in Belarus, Ukraine and Russia to ensure that there was benefit to not only the wider scientific community, but also to the patients and to the local Institutes that were responsible for collection of the samples. The CTB is supported by the governments of Ukraine and Russia, with financial support from the NCI of the US, the EC, Sasakawa Foundation of Japan and the WHO. The CTB was the first tissue bank of its type, providing multi-format, pathologically assured, biological samples to international research groups, and an infrastructure to track and collate research results from each individual sample with the aim of establishing a data repository for studies taking an "integrated biology" approach to understanding the mechanisms that underpin development of thyroid cancer. The CTB currently holds information and samples from more than 4000 patients, and has issued in excess of 10,000 samples for research in over 30 research projects. The CTB provides a paradigm for biobanking in the "omics" era.

Research on the Aftermath of Chernobyl: Have Lessons been Learned?
Jonathan M. Samet, University of Southern California

This symposium on the occasion of the 30th anniversary of the Chernobyl nuclear power plant disaster provides an opportunity to consider the scope of what we have learned about carrying out meaningful research in such demanding circumstances. Natural and manmade disasters are all too common; data are inevitably needed to aid those affected and to assess hazards. Beyond the immediate need for such data, there may be opportunities to carry out research that will generate new knowledge that will benefit those affected by the disaster and have broader implications. The research covered in this symposium is illustrative: further insights have been gained into the cancer risks associated with radiation and new 21st century science techniques are now being applied to deepen mechanistic understanding. The long-term non-cancer consequences have been investigated less comprehensively, in spite of their acknowledged importance, but the results are clear in showing persistent effects. Five years after the Fukushima disaster, studies are underway of the general population and of workers with the aligned purposes of surveillance for health outcomes and of research. For both of these nuclear power plant disasters, and for other disasters, e.g., the Deepwater Horizon oil spill, there had not been advance planning as to how research might be implemented as expeditiously as possible and accurate exposure assessment proved challenging. One "lesson learned" repeatedly is the need for anticipatory planning; disasters do happen and, as illustrated by research in the aftermath of Chernobyl, much can be learned but opportunities may be lost by delayed and fragmented implementation of research.

SYMPOSIUM ORGANIZING COMMITTEE

Jonathan M. Samet, *Chair*
University of Southern California

Lawrence T. Dauer
Memorial Sloan Kettering Cancer Center

Amy Berrington de González
National Cancer Institute

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University of New Mexico School of Medicine (Professor Emeritus)

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HISTORY OF THE BEEBE SYMPOSIUM SERIES

The Gilbert W. Beebe symposium was established by the Board on Radiation Effects Research (now the Nuclear and Radiation Studies Board) in 2002 to honor the scientific achievements of the late Dr. Gilbert Beebe (National Cancer Institute). Dr. Beebe was one of the designers and key implementers of the epidemiology studies of Japanese atomic bombing survivors and organized and led investigations into the Chernobyl accident. The symposium is used to promote discussions among scientists, federal staff, and other interested parties concerned with radiation health effects.

The eleven symposia that have been held to date have addressed a wide range of topics related to radiation and health:

- Scientific Highlights of RERF Studies and Chernobyl Studies (2002)
- Psychological Consequences of Exposure to Ionizing Radiation (2003)
- Recent Developments in Radiation Risk Assessment (2004)
- Beyond BEIR VII (2005)
- Pre-and Post-Conception Radiation Exposure: Sensitivity of Gametes, Fetuses, and Children (2006)
- Sixty Years of ABCC [Atomic Bomb Casualty Commission]/RERF: Major Contributions and Future Studies (2007)
- Radiation as a Cause of Cardiovascular Disease (2008)
- Radiation Exposures from Imaging and Image Guided Interventions (2009)
- Scientific Advances in Radiobiology and Radiation Epidemiology, Implications for Radiation Exposure Regulations (2010)
- Tracking Radiation Exposure from Medical Diagnostic Procedures (2011)
- The Science of Responding to a Nuclear Reactor Accident (2014)

The focus of this year's symposium is on commemorating the 1986 Chernobyl nuclear reactor accident and discussing the achievements of 30 years of studies on the radiation health effects following the accident and future research directions. Focus will be given to studies published after the 2008 United Nations Scientific Committee on the Effects of Atomic Radiation report titled *Exposures and Effects of the Chernobyl Accident*.

There is scientific and policy significance of the proposed 2016 Beebe Symposium topic: Ongoing studies of the Chernobyl accident are improving the understanding of the health effects caused by the accident. They are also important for obtaining a fuller scientific understanding of radiation health effects and biology/genetics in general and for informing radiation protection efforts.

Email us at nrsb@nas.edu if you are interested in receiving information about future Gilbert W. Beebe Symposia.

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PHOTO GALLERY

Gilbert W. Beebe with Chernobyl Research Collaborators

Rev 1, October 26, 2016

Courtesy of Alfred Beebe, son