## ■ Radiation-Induced Damage not Immediately Apparent: Skips Numerous Generations of Cells

Two groups of researchers working independently have found evidence of delayed cell damage arising from alpha and X-radiation. The damage is not expressed in the immediate progeny of the affected cells but is evident in future cell generations. These preliminary findings have startled the scientific community and if the results are replicated may lead some scientists to question the accuracy of the current dose-response models for the risk of ionizing radiation to humans.

Alpha radiation is a high-linear energy transfer (LET) radiation while X-, beta, and gamma rays are types of low-LET radiation. Alpha rays penetrate only about 0.1 mm into tissue but their energy is concentrated along a narrow track, while the energy from low-LET radiation penetrates deeply but is dispersed within a greater area in the cell. Consequently, the damage to a cell is about twenty times higher from high-LET radiation than from low-LET radiation.

Previously, scientists believed that if an alpha particle hit the nucleus of a cell, the cell would be destroyed but that if the particle missed or glanced off of the nucleus, the cell would survive without any subsequent damage. The newly published study by the Medical Research Council (MRC) Radiobiology Unit in Oxfordshire, England refutes this hypothesis.

### Alpha-Radiation Study

Eric Wright, PhD, head of the division of radiation oncogenesis at the MRC Radiobiology Unit and his colleagues recently published a report in *Nature* (1), describing their study of mice irradiated with low doses of alpha-emitting particles. The researchers took blood marrow stem cells from the mice and subjected them to 25, 50, and 100 rad (0.25, 0.5, and 1 Gray [Gy]) of alpha radiation. Another group of mice cells was subjected to 300 rad (3 Gy) of X-radiation, while a third group was not subjected to any radiation in order to serve as a control group. Eighteen percent of the alpha-irradiated cells survived while only 5% of the X-irradiated cells survived. The surviving cells visually seemed unscathed and the alpha-irradiated daughter cells also appeared normal. The cells divided ten to thirteen times before mutations were seen.

According to Dr. Wright, this delayed mutation effect means that the initial alpha radiation produced a genetic instability at the molecular level. Through an as yet unidentified biological mechanism, the genetic damage was expressed many generations later in the form of chromosomal abnormalities: some of the chromosomes were twisted or fragmented, while others were abnormally small.

In contrast to the alpha-irradiated cells, the immediate daughters of cells that survived X-radiation showed mutations and the chromosomal abnormalities were the same as those present in the mutated parent. The level of chromosome abnormalities after X-radiation was 0.5% compared to a level ranging from 21%–28% in the progeny of alpha-irradiated cells. The level of chromosome abnormality in the control cells (those that received no radiation) was 2%. Dr. Wright notes that there is no significant difference between the 0.5% abnormality level observed in the X-rayed cells and the 2% abnormality level observed in the control cells.

Dr. Wright and his team were surprised by the high level of non-clonal abnormalities in the progeny of alpha-irradiated cells. They had expected to see only a very occasional clonal abnormality in cells surviving alpha-irradiation. The next step is to move the research from in vitro to in vivo mice studies and to initiate in vitro human studies. In vivo mice experiments are in progress but, according to Dr. Wright, it is too early to assess symptoms of instability. Dr Wright's group has also started conducting in vitro assays with human bone marrow stem cells. Dr. Wright cautions that it is not certain whether the genetic instability shown in mice will occur in humans.

### X-Radiation Study

Although the MRC Radiobiology Unit study did not show a delayed mutation effect in cells receiving X-radiation, two studies conducted by John Little, PhD and colleagues at the Harvard University School of Public Health in Boston, Massachusetts showed just such an effect (2,3). Dr. Little believes his group may have seen these effects with X-radiation because the researchers used a much higher dosage of X-radiation than that used in the MRC study.

In a study using Chinese hamster ovary (CHO) cells, Dr. Little and Wushou Chang, PhD found that the cells surviving 1200 rad (12 Gy) of X-irradiation demonstrated "a persistently decreased cloning efficiency." The authors coined the term "delayed reproductive death" to describe this phenomenon. "The cells from these progeny clones show a persistently elevated frequency of spontaneous mutations . . . for up to 95-100 population-doublings post-irradiation." Drs. Little and Chang conclude that "radiation induces a type of genetic instability among some surviving cells that results in a heritable mutator phenotype, and that this instability may also be involved in the phenomenon of delayed reproductive death."

Dr. Little believes that the delayed mutations observed are a result of "small-scale genetic changes rather than large deletions or rearrangements [of chromosomes]." "Given the high frequency of the phenomenon [reduced cloning ability] among clones isolated from cells surviving irradiation . . ., it seems unlikely that directly induced mutation in a gene or group of genes can explain the effect."

Dr. Little co-authored another study with colleagues at the Harvard School of Public Health (3), in which the researchers sought evidence that X-irradiation could produce a molecular instability in mammalian cells. They examined the rate of coincident mutations (independently arising mutations occurring at the same time) in progeny of X-irradiated human lymphoblast cells and found the rate to be 100 times larger than expected. The authors conclude that "these results may provide the first molecular evidence that radiation can induce genetic instability that leads to a 'global' mutational process in mammalian cells."

The results from both the alpha-irradiated and X-irradiated cells support the hypothesis that genetic instability is occurring at the molecular level through an unseen biological mechanism. The extent of this instability and its effect on humans is not yet known but the preliminary findings have implications for the determination of the risk to humans from radiation exposure as well as exciting possibilities for use of the biological mechanism to aid in reversing or preventing genetic defects.

The primary source of alpha radiation for the public is radon, which is in the soil and often seeps into the basements of homes. Alpha radiation is also emitted by plutonium, which is used in the creation of nuclear weapons by the defense industry and in nuclear power plants. Workers in these environments have a potential exposure to alpha radiation. The primary sources of X-radiation are the soil (background radiation) and diagnostic X- and gamma rays administered in health care facilities.

Epidemiological studies show that certain doses and types of low-LET radiation induce cancer, especially leukemia, which is the most common radiation-induced malignancy. Dr. Wright and his colleagues believe their data may lead to a reassessment of the potential of low doses of high-LET radiation to contribute to carcinogenesis. ". . . If as we believe, . . . there may be classes of unique radiogenic damage induced only by high-LET radiations, then the RBE [relative biological effectiveness] for such damage would be effectively infinite. Leukemias arising from such a situation may not have been identified as radiogenic from human epidemiologial data (which is based predominantly on considering low-LET radiation) and our findings may then have considerable relevance to the problem of low-dose radiation exposure from artificial or natural alpha-emitters."

In an editorial accompanying the MRC article in *Nature* (4), John Evans of the MRC human genetics unit in Edinburgh, England noted the potential effect of the new data on the radiation dose-response risk models currently used. "One concern for radiation protection is the nonuniformity of absorbed dose. For instance, it is difficult to evaluate the consequences of the deposition of a 'hot' particle in a sensitive tissue. An alpha-emitting speck of plutonium will have a high probability of killing cells in its immediate vicinity, but if it engendered instability in nearby surrounding surviving cells its effect would be very much greater than that predicted on the total body dose received."

Arthur Upton, MD, chairman of the department of nuclear medicine at New York University Medical Center, New York City and chairman of the National Research Council's fifth Committee on the Biological Effects of Ionizing Radiation (BEIR V committee) is intrigued by the alpha and X-irradiation studies' results. While he believes the research will add to the body of molecular knowledge, he does not believe that it presents any evidence that would lead the BEIR committee to revise its radiation risk estimates. He says that "it is not clear that the new findings modify the risk assessment made by the BEIR IV and BEIR V committees." He notes that the BEIR IV and V committees conducted long-term studies of the carcinogenic effects of radiation in both experimental animal trials and in human subjects (tracking the health of the atom-bomb survivors and the genetic effects on their children). He believes that any effects of the radiation, both direct mutations and delayed mutations, "have had a chance to express themselves."

Dr. Upton notes that the BEIR IV and V committees also studied the effects of alpha radiation on uranium miners and dial painters, measuring the amount of radon deposited in their skeletons. Thus, he feels that the carcinogenic risk from alpha radiation has already been adequately addressed.

To Dr. Upton, the real value of the new studies is the door they open to new knowledge at the molecular level. "The real benefit of this research is to help us understand the mechanisms involved." As the biological mechanisms that control normal and abnormal gene expression become better understood, that knowledge can be used by physicians to treat disease.

**Joan Hiam**
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## New Hazardous Waste Containment Method Encases Waste in Glass

In situ vitrification turns hazardous waste into an obsidian-like mass. *Courtesy of Battelle Memorial Institute's Pacific Northwest Laboratories.*

Scientists at Battelle Memorial Institute's Pacific Northwest Laboratories (PNL) in Richland, Washington have devised a method for isolating radioactive and toxic waste from the environment for hundreds of thousands of years. In the process, known as vitrification, electricity is used to heat the soil and waste material to extremely high temperatures until it fuses into a molten mass. The waste and soil are then allowed to cool (this process can take up to a year) into an obsidian-like mass. At this point, the organic wastes have been destroyed and the inorganic wastes are dissolved into and encased within the glassy rock.

Scientists at Batelle have experimented with two types of vitrification processes. The first type, in situ (on-site) vitrification, is used in cases where the waste is spread out over a large area of soil. A number of electrodes are placed vertically in the ground and an electric current is run among them until the soil is heated to 1,700 °C–2,000 °C. This process can take from 3–7 days, depending on the viscosity of the soil and rocks and the type of waste stream. A hood over the site collects hazardous gases and dusts, which are sent via pipe to an off-gas treatment system. The current is then shut off and the vitrified waste cools into a crystalline structure. The glassy rock creates a barrier between the waste and the underlying soil and water table.

The second method of vitrification is used when the waste is being stored in containment tanks in either solid or liquid form. The waste is fed into a ceramic melter, which may be at a distant location or may be built on-site. Within the ceramic melter, the waste is mixed with glass-forming chemicals and an electric current is run through electrodes to raise the temperature to 1,200 °C–1,500 °C. Convection is carefully controlled to make sure the waste is circulating properly and thus receiving uniform treatment. After 2–5 days, the waste is allowed to cool. An off-gas treatment system captures any hazardous gases or dust particles and returns them to the ceramic melter for further processing.

The vitrification process is currently being used on an experimental basis at a number of U.S. nuclear weapons or fuel reprocessing facilities owned or operated by the Department of Energy (DOE). Pilot projects are in progress at the Hanford nuclear reservation in Washington, the Savannah nuclear power plant in South Carolina, and the West Valley fuel reprocessing plant in New York. (This plant was shut down a number of years ago.) The DOE plans to have ceramic melters operating on a large-scale basis at all three of these facilities by the end of this century, according to Chris Chapman, a staff engineer with the Waste Treatment Technology Department at PNL.

The DOE's current plan is to store the vitrified waste at the Yucca Mountain underground repository in Nevada and at the Waste Isolation Pilot Plant in New Mexico. Neither of these sites has yet accepted any nuclear waste due to opposition by state officials in Nevada and New Mexico. However, it is possible that vitrified waste will encounter less local political opposition.

A number of foreign governments are already using vitrification, some on an experimental basis and others as an integral part of their waste disposal strategies. Germany is using ceramic melter vitrification for its high level nuclear waste, which will then be stored in an underground repository and Japan expects to start a similar vitrification program imminently. England has recently started a ceramic melter vitrification operation while France has been using vitrification technology since 1979.

Japan has found an additional use for the vitrification process. The government is experimenting with creating vertical columns of vitrified rock on steep hillsides that are prone to erosion or mudslides. The pillars are melded onto the underlying rock strata providing a mudslide and rockslide barrier.

In the U.S., Batelle recently licensed its in situ vitrification technology to Geosafe, which plans to market the technology to commercial industries. Meanwhile, Batelle has licensed its ceramic melter vitrification technology for use only in medical waste vitrification to American Environmental Management Corporation (AEMC) of Stanton, California. The company is building a ceramic melter vitrification facility in Richland, Washington and expects to begin operation of the facility by February 1993. This plant will be the first commercial application of

ceramic melter vitrification technology in this country.

Although the facility will initially process only medical waste (excluding radioactive or hazardous waste), AEMC expects that in the future the plant will vitrify municipal waste as well. The plant will process 25 tons of medical waste per day and the vitrification process will reduce the waste to less than 1% of its original volume. After the Richland plant is in full operation, AEMC intends to expand its vitrification operations to other sites in the U.S. and in other countries.

**Joan Hiam**
Managing Editor, *JNMT*

## ■ News Briefs

### New Way to Order Society of Nuclear Medicine Books

The Society of Nuclear Medicine (SNM) has changed the way it fulfills book orders. All orders for books and pamphlets published by SNM should be placed directly with BookMasters, SNM's fulfillment center, rather than with the SNM central office. The changes were made in January 1992 following cutbacks at the SNM office in New York and should bring modest cost savings for the organization, according to David Teisler, director of publications. Although the transition may cause some initial inconveniences, Mr. Teisler expects the changes to speed the delivery of books by two or three days. Address SNM book orders to: SNM Book Order Department, BookMasters, Inc., 1444 State Rt. 42, RD 11, Mansfield, OH 44903. You may call BookMasters for a book order form or information at (800) 247-6553 or (419) 281-1802; Fax: (419) 281-6883.

### Physicians to Receive CME Credit for Technologist Program Continuing Education Courses

This year, most technologist continuing education courses have been approved for continuing medical education (CME) credit. All physicians are encouraged to participate. As usual, most of the educational sessions have been approved for VOICE credit. If you have any questions concerning CME or VOICE credit, please contact Ritone Ivaska at the SNM New York office.

### Technologist Section Awards

The following monetary prizes will be awarded to the recipients of 1992 Technologist Section scientific program awards. The winners will be announced and prizes presented at the 1992 SNM Annual Meeting in Los Angeles, California.

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| **Scientific Paper** | |
| First place | $500 |
| Second place | $300 |
| Third place | $200 |
| **Scientific Poster/Exhibit** | |
| First place | $200 |
| Second place | $150 |
| Third place | $100 |
| **Best Student Scientific Paper** | $100 |
| **Cardiovascular Council Awards Scientific Paper** | |
| First place | $500 |
| Second place | $300 |
| Third place | $200 |

## TECHNOLOGIST JOB NETWORK

The New England Chapter—SNM/TS announces **"The Job Hotline,"** a national toll-free, hotline for nuclear medicine. The hotline is designed to provide a quick link for technologists seeking jobs and for hospitals seeking technologists. Institutions seeking technologists should call the hotline number, leave the name of the institution, title of the job opening, and name and number of the contact person; data are then stored for three months in a database for anyone who calls the hotline seeking employment. Technologists seeking employment should call the hotline number, specify state(s) which are of interest, specify type of job desired, and leave name and address. A listing will then be sent out in 48 hours; all inquiries are kept confidential. If an opening has not been filled within three months, the institution should call again to have it listed. The institution should also call if an opening has been filled so that it can be deleted from the database. The hotline numbers are **1-800-562-6387 (1-800-JOB-NETS)** or **1-990-4212 in Maine.** Questions or comments should be directed to: Tom Starno, Manager, Job Hotline, New England Chapter—TS at **(207) 945-7186.**

The Mideastern Chapter—SNM/TS will provide a referral network for technologists seeking employment and for hospitals in need of technologists. Interested individuals should call Cathy Gonzalez at **(301) 855-1712.** Please leave your name, address, phone number and a brief description of your request.

## EDITOR'S NOTE

SNM chapters are invited to submit job referral service listings for publication. Pertinent information—name and brief description of the service, telephone numbers and/or address, name or number of contact person for inquiries—should be sent to: Leigh Silverman, Section Editor, *JNM/JNMT,* Society of Nuclear Medicine, 136 Madison Avenue, New York, NY 10016-6760.