Number Four 1986

Oak Ridge National Laboratory review

ORNL Takes Root in the West

THE COVER: ORNL has taken root in the Grand Junction valley in Colorado, where employees have been supporting a Department of Energy effort to survey properties to determine whether they are in need of decontamination. See article on page 1.

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The *Review* is published quarterly and distributed to employees and others associated with the Oak Ridge National Laboratory. The address of the editorial office is: Building 4500-North, Oak Ridge National Laboratory, P.O. Box X, Oak Ridge, TN 37831. Telephone: Internal 4-7183, Commercial (615) 574-7183, or FTS 624-7183.

ISSN 0048-1262

Oak Ridge National Laboratory

review

VOLUME 19 **NUMBER FOUR 1986**

DEPARTMENTS

OAK RIDGE NATIONAL LABORATORY

operated by Martin Marietta Energy Systems, Inc. for the Department of Energy

View of the Grand Junction valley from the top of Colorado National Monument. The valley is adjacent to Grand Junction, where ORNL employees have been surveying properties to determine whether they should be cleaned up by DOE's uranium-mill tailings remedial-action program.

Sizing Up Contaminated Properties:

A Saga of ORNL's Western Pioneers

By CRAIG LITTLE and BARRY BERVEN

Go west young man, go west!
—Horace Greeley

Over the years, a number of folks on this continent have felt the reverberations of that cry. Most have sought fame and fortune in the western United States, but others have looked for a new challenge or chance to succeed. Not many Oak Ridgers know it, but for the last couple of years Oak Ridge National Laboratory has had some pioneers out west. They also sought a challenge, but one of a different kind.

Where many pioneers sought instant success or wealth, these staff members established a new ORNL office. This article briefly describes why they went, what they are doing there, and what has been gained by their presence in the West.

The Problem

In 1983, Ogene Jennings, Hal Jennings, Craig Little, John Roberts, and Dave Witt of the

Craig Little is the manager of the Grand Junction office for ORNL's Health and Safety Research Division (HASRD). He came to ORNL in 1976 after receiving a Ph.D. degree in radioecology from Colorado State University. In addition to work in environmental waste management, his research efforts have ranged from radiation protection to modeling environmental transport of various pollutants. Little serves on the Manpower and Professional Education Committee of the Health Physics Society.

Health and Safety Research Division and Tom Barclay of the Instrumentation and Controls (I&C) Division moved to Grand Junction, Colorado, to meet a challenge. Their mission was to establish a new home base for part of the Uranium Mill Tailings Remedial Action (UMTRA) Project sponsored by the U.S. Department of Energy. The UMTRA project was established after Congress passed the Uranium Mill Tailings Radiation Control Act of 1978, which mandated that inactive mill tailings piles and associated properties should be cleaned up or made safe for habitation. After the U.S. Environmental Protection Agency (EPA) set standards for cleanup of the associated or vicinity properties, ORNL was commissioned by DOE to conduct some preliminary surveys. The purpose of those preliminary surveys is to recommend to DOE whether to clean up individual properties.

Nationwide, more than 10,000 vicinity properties are considered contaminated enough to require that they be surveyed by ORNL. (See map of the United States showing mill sites.) How did so many homes, businesses, and public

Employees at ORNL's new office in Grand Junction, Colorado, have surveyed hundreds of radon-emitting properties for DOE's Uranium Mill Tailings Remedial Action Project. In addition, the office is responsible for several administrative and technical innovations that are expected to save the project millions of dollars.

The original six western pioneers from ORNL are, from left in back, Tom Barclay (Instrumentation and Controls Division), Hal Jennings (Chemical Technology Division), Dave Witt (Health and Safety Research Division); from left in front, John Roberts, Ogene Jennings, and Craig Little, all of the Health and Safety Research Division. Hal Jennings and Ogene Jennings are husband and wife. In a little over a year, this staff of six expanded to 65 people, and the annual budget grew from $1.2 million to $7 million.

Barry Berven is leader of the Radiological Survey Activities (RASA) Group in HASRD. The Grand Junction work is one of several projects in RASA that assess radiological and chemical contaminants at sites throughout the United States (including the local facilities). A native of Colorado, he received his Ph.D. degree in health physics in 1979 from Colorado State University. His research interests include environmental radiological surveillance; detection of radiological, chemical, and hazardous wastes; and radiation protection education. Here, Berven and Ogene Jennings review the budget plans for subcontracts with ORAU and Bendix Field Engineering Corporation.

places become contaminated? The answer to that question lies in the characteristics of the tailings themselves and the process of producing the uranium so necessary to the Manhattan Project and nuclear power itself.

Most of the commercially used uranium mined in this country was extracted from deposits in the West. The crusty prospectors of earlier days gave way to trained geologists, who used more sophisticated methods of finding the ore. As a result, hundreds of mines once operated in the Western states, principally Colorado, New Mexico, Arizona, Utah, Wyoming, and South Dakota. The ore was mined like any other: find the deposit or vein and dig it up. However, uranium ore, like gold ore, contains only a few percent by weight of the desired metal—the rest is just rock.

Once the ore has been removed from the ground, it has to be milled to separate the uranium from all that excess rock. That separation is done at a mill. To mill uranium, the ore is crushed to a sandy consistency and treated chemically. Often the treatments relied on some type of acid. At other mills, the ore was heat-treated in a cracking process. The one common thread, though, was the by-product of the milling process: tailings.

Depending on the process, tailings are sandy materials colored pink, brown, or gray. Millions of tons of tailings were left behind after the ore was milled at the 24 sites being cleaned up by the UMTRA project. The leftover sand, or tailings, was a problem for many of the mill operators. It piled up and got in the way of their process. So, in many of the nearby towns, the tailings were literally given

Location of the former mill sites in the UMTRA Project.

Most of the ORNL and ORAU staff members in the DOE Grand Junction Office bundle up for a group photograph.

away for whatever use could be made of them.

Being sand-like, the tailings were used for just about everything imaginable: in mortar, in material to fill low spots in yards, in cement mixtures to make concrete, or in children's sandboxes. Because the natural soils in western Colorado are very alkaline, the slightly acidic tailings were also often used as a soil conditioner to help produce greener, healthier lawns. Ironically, material once used to help the desert bloom is now considered a detriment to human health.

In some towns more tailings were used than in others. Grand Junction was undergoing a building boom during the time the mill operated, so free sand was a very popular commodity. Grand Junction also had a relatively large and long-lived mill; in fact, from 1950 through 1966, more tailings were hauled away from that mill for use by local people than from most of the other mills combined. Not surprisingly, of the 10,000 properties identified for further investigation, 8,000 are in Grand Junction.

The health risk of the tailings material comes not from the uranium itself, but from its decay products, radium-226 and the radioactive noble gas radon-222. Because the milling process was specific for uranium, the tailings material is relatively enriched with radium, uranium's major long-lived decay product. Radium is a natural constituent of all soils but exists in lower concentrations naturally than in tailings. The predominant health risk, however, comes from the decay products of the radon gas, such as lead-210, bismuth-214, and polonium-218. Generally called radon daughters, these isotopes attach to microscopic, dust particles. When inhaled, these radioactive particles may lodge in the lung or be absorbed through the lung into the bloodstream, which ultimately deposits them in the bone. Therefore, high concentrations of the inert radon gas may ultimately lead to either lung or bone cancer.

Fortunately for most Westerners and for the project, many of the mills were located in sparsely populated regions such as Monument Valley, Arizona. But the mill in Grand Junction and the one in Salt Lake City pose problems for densely populated areas. The magnitude of the problem in Grand Junction is the major reason that the ORNL office was opened there.

Kathy Dickerson, ORNL field team leader, uses a hand-held radiological monitoring device to detect radium in the foundation of a Western-wear shop in Grand Junction. Uranium-ore mill tailings were used as a construction material on private and public properties.

The Standards

The standards used to decide whether a property requires remedial action were written by the EPA. ORNL compares its measurements with the EPA standards before making a recommendation to the DOE-UMTRA project office in Albuquerque, New Mexico. Given the complexity of many of today's regulatory guides and standards, these EPA standards are relatively simple. In general, these guidelines are based on the calculated health risk from inhaling radon gas.

The outdoor standard decrees that the concentration of radium-226 may not exceed 5 picocuries/gram (pCi/g) above background in the top 15 cm of soil or 15 pCi/g in any subsequent 15-cm layer of soil. Both of these values must apply to an area of 100 m^2 and a total volume of 15 m^3. The indoor standard is slightly more complicated. Either an exposure rate of 20 μR/h above background (about three times the average background level) or a radon daughter concentration of 0.02 working level averaged over an entire year indicates sufficient contamination to require remedial action.

As with any set of standards, the person making the measurements must make some judgments. Subjectivity is especially required for the surveys conducted by ORNL's Grand Junction office. Because of the large number of properties that by law must be assessed in five years, the surveys are relatively superficial on purpose. To keep the cost per survey at a minimum, the number of various types of measurements is kept low. Thus, the members of the radiological survey teams are under above-average pressure to make correct judgments.

Given the external stimuli that sometimes exist on properties, maintaining concentration to make good judgments can be a challenge. For example, the team members who surveyed the Adult Bookstore in June 1986 had trouble even keeping their eyes on the meters, not to mention concentrating on the sometimes minimal fluctuations of tone in their earphones. Snarling dogs tend to make the mind wander, too!

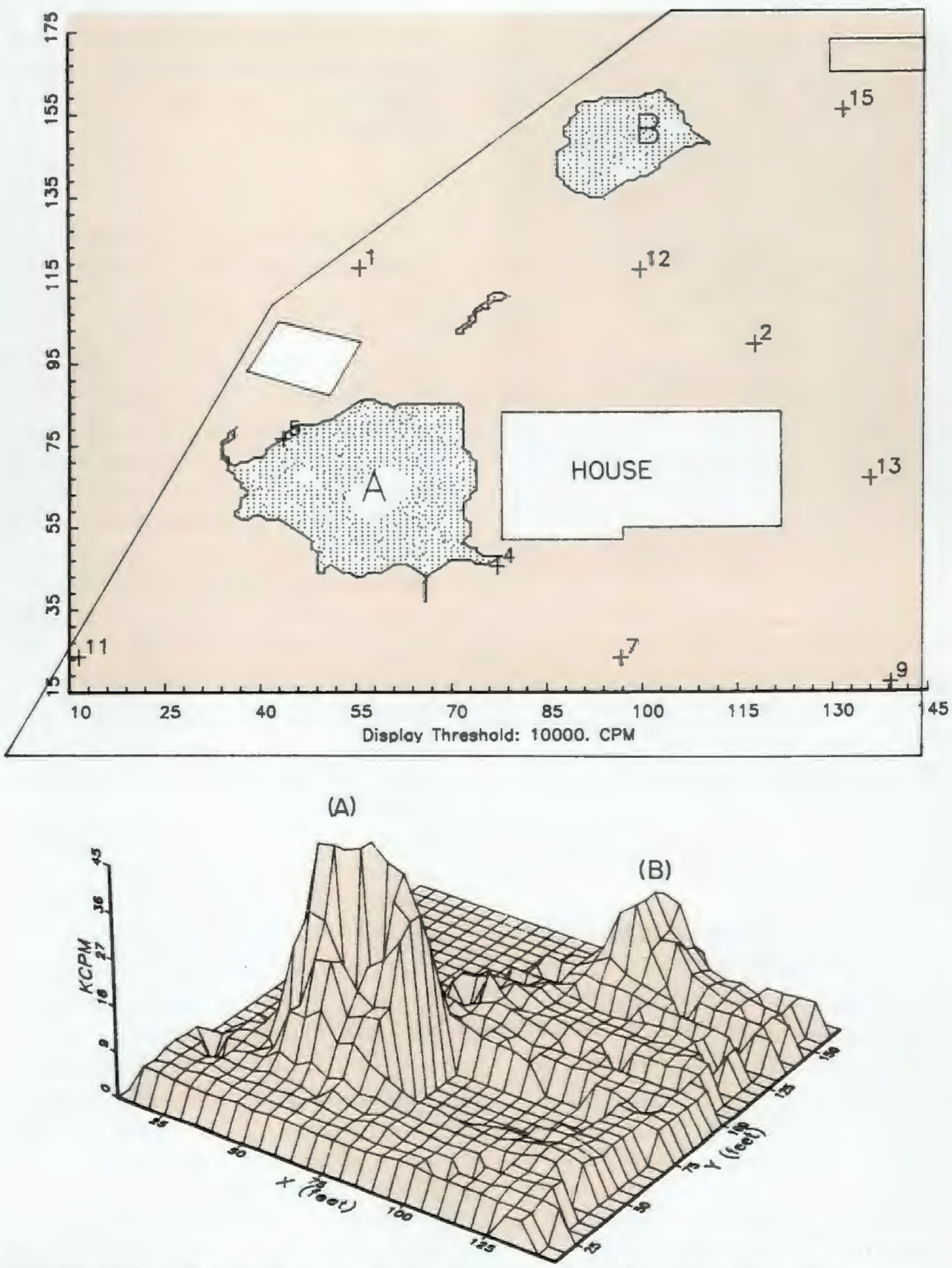
The Process

The prospects for the initial group of ORNL staff members in Grand Junction were a challenge, to say the least. All they had to do was move west, open an office, staff it, train the staff, and then conduct 10,000 surveys of private and public properties in 11 states in five years. Easier said than done. But doable.

The office was established at DOE's Grand Junction Project Office compound. The operating contractor for the facility was then Bendix Field Engineering Corporation, a subsidiary of Allied-Bendix, which Martin Marietta Corporation had unsuccessfully tried to purchase in 1982. Since October 1, 1986, the Grand Junction compound has been managed by UNC Technical Services, Inc. The ORNL-UMTRA office is headed by Craig Little, who reports to Barry Berven, head of the Radiological Survey Activities Group at ORNL.

The staffing and training were among the most important aspects of the project. With the assistance of the personnel office in Oak Ridge, the hiring process was streamlined by conducting interviews and processing information in Grand Junction. Because of uncertainty regarding the number of staff members that would ultimately need to be hired, an agreement was reached with Oak Ridge Associated Universities (ORAU) whereby they would hire staff as needed. At least half of the more than 60 staff members at ORNL's Grand Junction office are employed by ORAU.

The process of making a recommendation of remedial action to DOE by ORNL is highly



Results of the radiological survey of a private property in Grand Junction, Colorado, using USRADS. Contaminated areas (A and B) are shown in two- and three-dimensional plots.

Gretchen Smith uses a gamma scintillation detector to survey the property outside a Grand Junction warehouse.

structured. It includes acquiring consent to survey from each property owner, developing maps of the properties to be surveyed, conducting a radiological survey, analyzing soil samples, reducing and storing data, and writing a report. If any of these steps are not completed as scheduled, the entire process loses efficiency.

Acquiring consent for access is potentially the single most troublesome aspect of the project. Each property owner is notified individually by certified mail. If no response is received within 60 days, the owner is notified again by mail. As a last resort, telephone or person-to-person contacts are made. In Grand Junction, especially, property owners may be apathetic or even hostile to the project. Many Grand Junction residents have worked in uranium mines or mills or know someone who did. They often think that the project isn't worth the cost or bother. Some of them want the tailings there.

One property owner had recurrent water problems in his basement. As an employee of the mill in the 1950s, he had access to all the tailings he wanted, so he filled in his entire basement with them and solved his seepage problem that way! Another owner was convinced that radium gamma rays were good for him and kept a mattress-sized box of uranium ore underneath the bed in which he slept. Most property owners aren't so extreme.

Because the individual owners are unpredictable, the ability to obtain the necessary consents is also difficult to predict. To date, we have been remarkably successful in obtaining adequate numbers of consent forms. However, as the project continues, we anticipate increasing difficulty in achieving such successes. During the latter

Little reviews the status of inclusion survey reports for Shiprock, New Mexico. The reports recommend whether to include or exclude the surveyed sites for remedial action.

Debbie Barslund and Clarence Guyer of ORNL at one of ORNL's three trailers at the DOE-Grand Junction compound.

portions of the project, the staff's knowledge of UMTRA and the Grand Junction community coupled with their charm and tenacity will continue to make the ORNL portion of the project successful.

Once a property owner has consented to a radiological survey, land surveyors visit the property to make a base map drawing. The drawing serves as a template for the radiological survey team. By having the drawing in hand before the radiological survey, the team leader can better plan the survey and can easily record the location of any contamination detected on the property.

The radiological survey is conducted as soon as possible following the land survey. Because the radium decay products from uranium tailings give off gamma rays in levels proportional to their concentrations, radiological surveyors use gamma detectors to determine whether hazardous levels of these substances are present. Teams do a complete gamma scan of the property and shade the drawing to indicate where contamination is found. Sometimes determining the location of the contamination is easier said than done. At one residence, the property owner had recently undergone a nuclear medicine diagnostic test that introduced a radioactive substance into his body, thus making him "detectable" by hand-held gamma detectors. At the end of the survey, while comparing and rechecking notes, the team members realized that his "body burden" had greatly influenced their readings. What might have been written up as a contaminated property was instead found to be a temporarily radioactive owner of a clean home.

Frequently, soil samples are taken to make a determination of the need for remedial action. Indoors, instantaneous measurements of the radon-daughter concentration (RDC) may be made. For properties in which the decision about whether to recommend cleanup is most difficult to make, an annual average measurement of the RDC may be made. Annual average measurements are made only as a last resort, because they delay the final recommendation.

Soil samples collected on the property are analyzed in a mobile laboratory housed in two semi-trailers parked inside the Grand Junction Project Office compound. Soil-crushing and drying apparatuses are housed in one trailer, and the sodium-iodide well crystals that detect the radon daughters are contained in the other. As many as 600 samples a week may be analyzed by this system.

The data resulting from analysis of the samples are collated by the team that conducted the survey. A simple letter report that follows an approved format is written and reviewed by another team and a group of technicians serving as editors. A cover letter is attached and the entire package is submitted to DOE for consideration.

If DOE agrees that the level of contamination of the property exceeds EPA standards, then the property is included in the program and the remedial action contractor, either UNC, Inc., or MK-Ferguson, proceeds with engineering design and construction. If the property does not exceed the remedial action guidelines, the property owner

A HASRD Radiological Survey Activities team collects a soil sample in Grand Junction during a radiological survey for DOE's Uranium Mill Tailings Remedial Action Project. Team members are, from left, Gretchen Smith of ORAU, Chris Muhr of ORNL, and Mike Roche of ORAU. The project has evaluated about 3000 properties for the presence of uranium-ore mill tailings.

The Colorado National Monument looms in the background of ORNL's Grand Junction office.

receives a copy of the ORNL radiological survey report with a cover letter from DOE explaining that the property is not eligible for remedial action.

Any remedial action required is financed entirely by the UMTRA project at no cost to the property owner. Engineering, assessment, and construction are funded 90% by DOE and 10% by the appropriate state.

So far in the surveys, the teams have found that about 50% of the properties examined are contaminated and have recommended their inclusion in DOE's remedial action program.

Progress to Date

From the ORNL perspective, progress on the UMTRA project takes several forms. First and foremost to DOE is the recommendation milestone plan. Progress of a secondary nature is measured in terms of spin-off technologies or methodologies. In both categories ORNL's Grand Junction office has been very successful.

The milestones of the UMTRA project are specified in terms of the number of remedial actions completed. However, before a property can be cleaned up, ORNL must survey it to see if the EPA standards are exceeded. Only about 50% of the properties surveyed qualify for remedial action. During fiscal year (FY) 1984, the first year that ORNL's Grand Junction office existed, only 485 radiological surveys were conducted. That year was largely devoted to establishing the office and hiring a small staff. During FY 1985, however, explosive growth in the staff occurred; the four-fold increase in staffing resulted in more than 1600 surveys and recommendations. Even though FY 1986 has seen less staffing growth, the Grand Junction staff completed more than 3100 recommendations. ORNL's office in the West has consistently delivered more than the planned number of recommendations. In fact, recommendations were accomplished 6% ahead of the plan for FY 1986.

Another aspect of milestone performance is cost. While being ahead of schedule, ORNL has also been below projected (funded) cost. During FY 1985, ORNL returned $143,000 to the UMTRA project office to support other work.

ORNL's Grand Junction office has also made technical progress on the UMTRA project. The vast amounts of data collected and stored have required efficient methods of data management. Consequently, a local area network of more than 35 IBM-PC, IBM-XT, and IBM-AT computers has been developed and installed. This local area network is the largest of those now at ORNL. We use the data-base manager KnowledgeMan, a powerful package of computer programs, to store the data and retrieve desired information.

Another administrative innovation within the UMTRA project is the use of computer-assisted drafting (CAD). ORNL's office in the West has installed a number of CAD stations that use the AutoCAD software package to draw the base maps of properties required for the survey teams. These drawing files are transported to the remedial action contractors, who find them easier to store, retrieve, and amend than hard copies. Use of CAD is projected to save the UMTRA project several million dollars during the life of the project.

The most exciting technical spin-off from ORNL's Grand Junction office has been the development of the ultrasonic ranging and data system (USRADS). This system, currently being field tested, promises to save the UMTRA project as much as $20 million if used by the remedial-action contractors.

Briefly, USRADS uses ultrasound transmitted from a surveyor's position to as many as 15 perimeter receiving stations located around the property being surveyed to establish that position with respect to those stations. In conjunction with the ultrasound, radiofrequency (RF) transmission signals from the surveyor's backpack initiate the start time of the ultrasound as it leaves the surveyor's location and an RF stop signal is sent from each perimeter receiving station as it hears the ultrasound. A microcomputer nearby is equipped with RF receivers to obtain the start signal and the stop signals. The surveyor's location (within 15 cm, or 6 in.) is calculated each second by triangulation using the time-of-flight of the ultrasound.

In addition to the positional information, the detected gamma exposure rate is also transmitted from the surveyor to the computer each second. The computer processes these signals to correlate the surveyor's exact position with the radiation data collected. The combined gamma and positional information can be used in many ways to limit the need for data analysis by slower, less accurate methods. USRADS works over a 2-ha (5-acre) area.

USRADs was developed in the Research Instrument Section of the I&C Division by a working group under the direction of Mike Blair. At last count, at least ten I&C staff members had contributed to the development of this system for which a patent is being sought.

Besides radiological surveys, USRADS has numerous potential uses such as hazardous-waste characterization, land surveying, and robotics control. Effectively, any sort of measurement device that produces an output signal can be fitted to a backpack to transmit information to a computer. Only the imagination of the developer limits the potential uses of this device and its subsequent adaptations.

The Future

The ORNL office in Grand Junction, which is now fully staffed by 65 people, is performing well for the UMTRA project. However, this project has a finite lifespan. As with any project, the staff has apprehensions regarding the future. The question on everyone's mind (especially those hired and located in Grand Junction) is, "Where do we go from here?"

Since the founding of the office, and even before, that question has been asked. Knowing the uncertainties in funding, especially when a single agency or project is involved, the ORNL-Grand Junction staff has a right to be concerned.

The hope of the management of the Grand Junction office is that our recently hired and trained multidisciplinary group of environmental professionals will be requested to work on other projects. The flexibility and willingness of the entire ORNL staff in Colorado to rise to a challenge will certainly be expressed in further successes just as the eagerness of earlier pioneers led to the settling of the great American West. ornl

Searching for the "quark-gluon plasma"

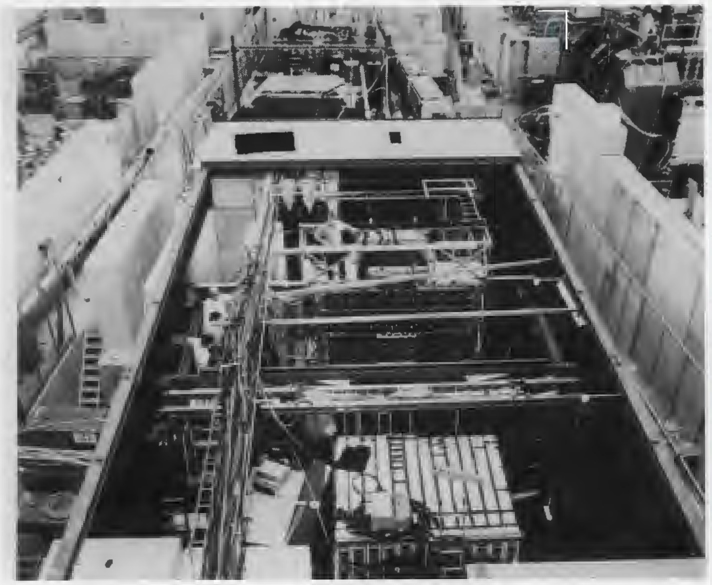
ORNL physicists in late 1986 participated in an international experiment in Switzerland aimed at creating a new state of nuclear matter—the "quark-gluon plasma." They also developed and installed calorimeters for one of five experiments, WA80, at the CERN accelerator complex in Geneva. The devices performed well.

On November 20, 1986, CERN experimenters, including ORNL's Terry Awes, Dick Cumby, Bob Ferguson, Felix Obenshain, Frank Plasil, Soren Sorensen, and Glenn Young, began the first two-week stage of the WA80 experiment. Accelerated nuclei of oxygen were collided with target nuclei of carbon, copper, silver, and gold at energies of 3.2 trillion electron volts. This energy, which is about 10,000 times higher than can be attained at ORNL's Holifield Heavy-Ion Research Facility, is the highest energy ever reached by accelerated nuclei.

The ultimate goal of the program is to achieve a new state of matter—the quark-gluon plasma—which is the primordial state from which all known particles are thought to have condensed a few instants after the Big Bang (a theoretical explanation of the formation of the universe). Some 300 scientists from about 60 institutions and 18 countries are involved in this research.

The first experiments were completed early in December 1986. In a graphic demonstration of the conversion of energy into matter, the ORNL team observed a record 400 charged particles produced in a collision between nuclei of oxygen and gold in which the initial number of charged particles—protons—is only 87. It was also observed that high energy densities are achieved during the collisions. For many scientists at CERN, this result was gratifying because of the concern that nuclei at these velocities may merely pass through each other without creating the region of high temperature and density needed for the formation of the quark-gluon plasma.

From preliminary results, the highest energy density achieved in this first run was about two-thirds of that required to form the quark-gluon plasma, according to recent estimates. Says Plasil: "Although the theoretical predictions of the required energy density are not highly reliable in a quantitative sense, the prospects appear to be nevertheless encouraging for creating the plasma this year, when heavier calcium or sulfur projectiles become available at CERN."



An overview of the international WA80 experiment at the CERN laboratory in Switzerland, which aims at creating a new state of nuclear matter. The beam direction is from the top to the bottom of the photograph. The large cube in the lower center is the wall calorimeter, designed and built at ORNL.

Advanced Control Test Operation planned for ORNL

Human error has been said to be the primary cause of the world's two most severe nuclear reactor accidents—at Three Mile Island and Chernobyl. One promising way to minimize human error is the use of advanced control systems that give operators an early diagnosis of reactor problems and suggest how best to deal with them.

An ORNL project, begun with Laboratory seed money but now being funded by DOE, will develop such systems. The Advanced Control Test Operation (ACTO) project is expected to become a major program that will be housed in a new facility, whose planned location is north of and across the road from the Holifield Heavy-Ion Research Facility. The total program cost is estimated at about $90 million.

The purpose of ACTO is to ensure that the reactor industry benefits from advances in digital control technology. According to Syd Ball of ORNL's Instrumentation and Controls Division, reactors having more intelligent and fault-tolerant advanced controls could reduce the number and duration of outages, prevent incidents from becoming accidents, and improve the overall operating performance of reactors. In terms of the expected payoff, a 1% increase in U.S. reactor availability would result in utility savings equivalent to the cost of a new large plant. Currently, the average U.S. nuclear power plant is available only 56% of the time—far less than those in most other nuclear nations.

ACTO will include plant dynamic simulations as well as control systems consisting of computer hardware and software. Robert Uhrig, an ORNL-UT Distinguished Scientist, is working on this project along with Syd Ball, Les Oakes, Bob Shepard, and others.

ACTO would also incorporate advances in artificial intelligence. Uhrig has written, "The world might never have heard of Three Mile Island if [it] had been equipped with an artificial intelligence diagnostic system to quickly evaluate the reactor's unexpected behavior and recommend corrective action. Although we know little about the Chernobyl accident, it is possible that it too could have been prevented by the use of AI."

Another Large Coil Program milestone reached

On November 6, 1986, the last of six test coils in the Fusion Energy Division's International Fusion Superconducting Magnet Test Facility was operated at full design field and current. This coil, made by the Westinghouse Electric Corporation, reached a maximum field of 8 tesla, or 150,000 times the strength of the earth's magnetic field, with a current of 18,000 amperes. The other five magnets contributed to the field of the Westinghouse coil. This coil is the test facility's only superconducting magnet that contains niobium-tin conductor (the other five magnets have niobium-titanium conductor).

All coils have performed well so far, standing up to the stresses imposed by the background magnetic field. The Westinghouse coil was later tested to determine its tolerance to internal heating.

In December 1986, a pulsed magnetic field was applied to determine performance of the test coils under tokamak conditions. In a tokamak, the toroidal magnetic fields, which operate in steady state, are subjected to pulsed fields. The current experiments are designed to simulate this effect using a conventional copper coil positioned in the bore of a superconducting coil; the copper "pulsed coil" is moved from one superconducting coil to another. The successful operation in December of a new remote-controlled device to move the pulse coil was considered an engineering feat and was credited with keeping the research program on schedule.

The United States supplied three of the magnets, built by General Dynamics-Convair Division, Westinghouse, and—with help from Oak Ridge workers—General Electric. The foreign coils were made by Hitachi (for Japan), Brown Boveri (for Switzerland), and Siemens AG (for the European Atomic Energy Community, or EURATOM).

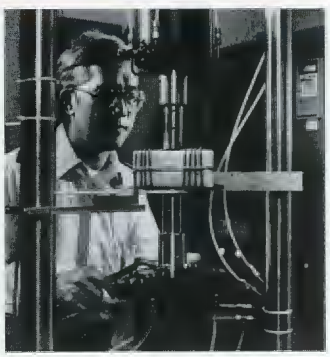
technology transfer briefs:

Instron acquires rights to ORNL testing device

An ORNL-developed device to test the strength of advanced ceramics has been licensed for commercial application to the Instron Corporation in Canton, Massachusetts.

In November 1986, Instron acquired the rights to use the "self-aligning grip assembly"—the first accurate and economical gripping device for measuring the tensile strength of advanced ceramics. The device was developed by Kenneth C. Liu of ORNL's Metals and Ceramics Division.

Martin Marietta Energy Systems, Inc., negotiated the agreement under a waiver of patent rights from DOE and claims no interest in the funds received under the licensing agreement. Instead, under a DOE-approved formula, royalties will be used by Martin Marietta Energy Systems to create a technology fund to



Ken Liu checks the device he developed for accurately measuring the strength of advanced ceramics. This self-aligning grip assembly has been licensed to Instron Corporation by Martin Marietta Energy Systems.

support development and transfer of other inventions having commercial potential.

William W. Carpenter, Energy Systems vice-president for technology applications, said, "This agreement successfully transfers to commercial use an ORNL technology that will have an important impact on the ceramic research community. The use of this unique device in research laboratories should greatly speed up further development of these materials."

Harold Hindman, Instron's board chairman, noted that "the agreement is an important step in enhancing Instron's role as preeminent manufacturer of testing instruments used for research in the rapidly growing advanced ceramics industry."

Unlike metal alloys, little or no accurate data exist on the tensile fatigue properties of advanced structural ceramics. Such data are vital for determining whether new toughened ceramics can withstand the severe operating stresses of advanced heat engines, for example. Conventional custom-made tensile fatigue testing devices are expensive and difficult to operate, require special specimen preparation, and frequently bend and damage specimens during testing.

The ORNL self-aligning grip assembly, which Instron refers to as the "Supergrip," provides extremely accurate specimen alignment and requires no special operator training or specimen preparation. Eight interconnected hydraulic pistons uniformly distribute a tensile load through the center of a test sample. The device can be water-cooled easily to make it compatible with induction heating or small furnaces, thus permitting higher-temperature testing of ceramic samples.

Support for the development has been provided by DOE's Ceramics Technology for Advanced Heat Engines Project of the Advanced Materials Development Program, which is administered by the Assistant Secretary of Conservation and Renewable Energy, Office of Transportation Systems.

Instron Corporation is a leading producer of instruments and systems used worldwide for advanced materials testing. ornl

Walderico M. Generoso is a senior scientist in ORNL's Biology Division, where he has worked since 1968. A native of the Philippines, he holds an M.S. degree from the University of the Philippines and a Ph.D. degree in genetics from the University of Missouri. He was a leader of the Environmental Protection Agency (EPA) Gene-Tox Working Group on Heritable Translocation Tests in Mice and of the International Commission for Protection against Environmental Mutagens and Carcinogens Working Group on Dominant-Lethal Tests in Rodents. He served as a member of the EPA Gene-Tox Committee on Risk Assessment and the National Academy of Sciences–National Research Council (Assembly of Life Sciences) Panel on Anticholinesterase Chemicals. Currently he is a member of the NAS-NRC (Assembly of Life Sciences) Panel on Cholinesterase Reactivators and of the NAS-NRC (Assembly of Life Sciences) Panel on Biomarkers of Reproduction. Generoso is a member of the editorial boards of *Mutation Research*; *Teratogenesis, Carcinogenesis, and Mutagenesis*; and *Journal of Molecular Toxicology*. He was senior editor of the book *DNA Repair and Mutagenesis in Eukaryotes* and co-editor of the books *Molecular and Cellular Mechanisms of Mutagenesis* and *Mutation, Cancer, and Malformation*. Here, Generoso examines mouse germ cell chromosomes in a microscope.

Genetic Risks of Using Ethylene Oxide

By WALDERICO GENEROSO

Mutagenic chemicals, substances that increase the rate of change in hereditary material, are widely distributed in the environment. The mutagens that attract the most attention are produced through human activity, but some are found in nature. Genetic risk to humans becomes a serious concern for chemicals to which humans are of necessity exposed and for which transmissible mutations in laboratory mammals, such as mice, have been demonstrated. In fact, many such chemicals exist, and among the chemicals that are already a part of the human environment, more will eventually be shown to be mutagenic.

For a decade or so, many new chemicals under development for possible use in drugs, cosmetics, or food additives, for example, have undergone one form of mutagenicity testing or another. When mutagenicity is clearly established and the chemical is of only dubious value, development is usually stopped. The dilemma arises when the chemical, either under development or already in the human environment, is of value to at least some segments of the society. It is a difficult challenge to determine the level of human exposure at which such a chemical can be produced and used economically without significantly harming human health. This task is the responsibility of the U.S. government and its regulatory agencies.

So far, these agencies have not carried out this responsibility with respect to genetic risk to future generations because of difficulty in interpreting the data. In the United States, no chemical has ever been regulated on the basis of its potential for increasing the mutation load of subsequent generations, nor have genetic risk evaluations contributed to regulatory decision making for any chemical.

Genetic Risk Assessment Today

That certain environmental chemicals can cause genetic damage

New ORNL studies on the mutagenicity of ethylene oxide suggest that regulations may be needed to limit brief exposures to the gas, which is widely used by health care workers to sterilize medical supplies. The study found that mice suffered more genetic damage when exposed to concentrated bursts of ethylene oxide than when exposed to low concentrations over a longer period. Already the study is playing a pivotal role in resolving regulatory questions about worker exposures to ethylene oxide. One study also led to a new discovery that calls attention to the possibility that, under certain conditions, women who are exposed to mutagenic chemicals on the day after conceiving may be unwittingly putting their future children at risk.

to reproductive, or germ, cells of experimental mammals is clear. The assumption that under certain conditions these chemicals are also likely to be mutagenic to human germ cells is not debatable. The most important aspect of the regulatory process is the accurate evaluation of genetic risk. Because direct study of chemically induced, transmitted genetic effects in humans is virtually an impossibility, this risk must be estimated from results of a variety of experimental test systems that are usually categorized into two groups—mammalian germ line and nonmammalian germ line. Consequently, several ways of evaluating genetic risk have been proposed. They differ from one another not only in how mammalian germ-line data are used but also in the amount of emphasis placed on nonmammalian germ-line data, such as those obtained in cultured mammalian somatic cells and the fruit fly, *Drosophila.*

Because no consensus exists on how chemical mutagens should be evaluated for genetic risk, an acceptable strategy and guidelines for preparing such assessments are crucially needed. This situation, which results in part from insufficient fundamental information, is being corrected at the Biology Division of Oak Ridge National Laboratory, where extensive research has been conducted on transmitted genetic effects of radiation and chemicals in mice.

Assessment of the genetic risk of an environmental chemical includes several components: (1) defensible evidence that the chemical in question has the potential to induce genetic damage in human germ cells, (2) identification and quantification in experimental systems of the types of mutations that are expected to be produced and transmitted to the next generation, (3) extrapolation of experimental results to humans (i.e., quantification of the increase expected for each class of mutation at human exposure levels), (4) estimation of the expected total contribution to the human genetic load, and (5) estimation of the impact on society of the mutational increase expected. This list is formidable. Whatever form an acceptable genetic risk assessment methodology takes, data on transmissible genetic effects in mice are indispensable.

Chemical mutagens may vary in the manner in which they react with various chromosomal components. Consequently, the types of genetic damage they produce may also vary. Because no single test system can measure every conceivable type of genetic damage, a number of methods must be employed to obtain data for gene mutations (dominant, semidominant, and recessive), small deficiencies, structural chromosomal anomalies (reciprocal translations, inversions, duplications, etc.), and numerical chromosomal anomalies (whole chromosomes missing or in excess). The magnitude of the problem is increased by the major influence of such factors as sex and germ-cell stage on both quality and quantity of mutations transmitted. Also, although established methods already exist for measuring many of the endpoints, easy applicable methods for measuring certain ones are still under development.

A Model Environmental Mutagen

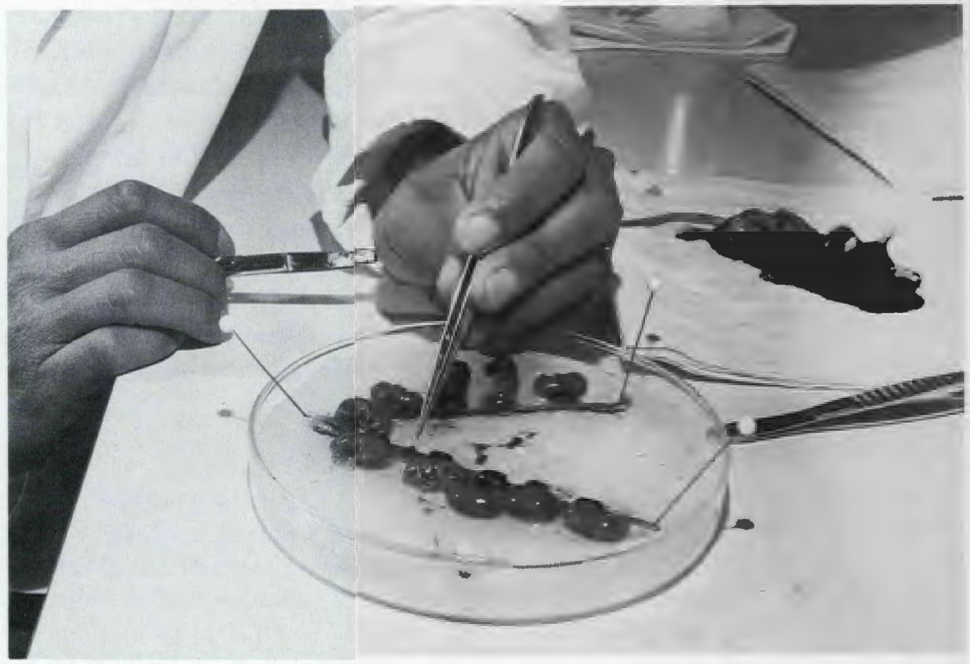
Data on transmitted genetic effects in mice are necessary, not only as a measure of endpoints that are considered directly in genetic risk assessment, but also as the standard for evaluating the usefulness of non-germ-cell effects as predictors in genetic risk assessment. To carry out a "real world" genetic risk assessment exercise, the Biology Division researchers are using the compound ethylene oxide (EtO) as the model environmental mutagen.

EtO, a colorless and odorless gas that has been found to cause mutations and cancer in animals, is produced on an industrial scale. In 1985, the EtO output in the United States was 2.6 billion kg (5.8 billion lb). The main bulk of EtO produced is used in organic syntheses such as production of ethylene glycol for air-conditioning units and the manufacture of acrylonitrile and nonionic surfactants. About 1% of the EtO consumed in the United States is used as a pesticide. It is used as a fumigant for foodstuffs and textiles and as an agricultural fungicide. However, the largest amount of human exposure to EtO, by far, takes place during sterilization of many types of hospital and laboratory equipment.

Before the Biology Division embarked on EtO mutagenesis research in 1978, the gas had already been found by others to be effective in inducing dominant-lethal mutations in male rats. Dominant lethals are primarily the result of chromosome breaks induced in parental germ cells; these breaks result in embryonic death early in gestation. Following this initial finding, the Biology Division has generated a large body of EtO data from risk-assessment-related research using mice.

In 1979, I found that EtO is effective in inducing dominant-lethal mutations in male mice regardless of whether it is administered by inhalation or by intraperitoneal injections (injections in the abdomen). However, I also observed that the response is restricted to a short segment of spermatogenesis—that is, it occurs only in late spermatids and early spermatozoa. In addition, I found that EtO produces heritable reciprocal translocations in these same germ cell stages. Heritable translocations result when two or more nonhomologous chromosomes exchange parts. Carriers of such translocations are either completely sterile or have reduced fertility. Rarely, other detectable expressions are also seen. I also exposed female mice to EtO and found a dominant-lethal response.

EtO clearly has the ability to cause chromosome breakage in certain germ cells. However, it does not appear effective in inducing point mutations, another type of genetic damage, in spermatogonial stem cells. Extensive specific-locus test data obtained by Liane B. Russell, Robert B. Cumming, and Patricia R. Hunsicker of the Biology Division showed EtO results to be negative in these stem cells, even though mice had been exposed for 80 to 115 days to a high concentration—255 parts per million (ppm).



Mouse fetuses are analyzed for developmental defects. The forceps points to an early embryonic death.

Thus, EtO has all of the properties of a model environmental mutagen from the standpoint of genetic risk assessment. It is a bona fide mammalian germ-cell mutagen; its production and use involve measurable human exposure; and, because it is socially and economically important, it is not likely to be banned altogether despite its mutagenicity and carcinogenicity.

Regulating EtO Exposure

As many as 200,000 health-care technicians may be exposed to EtO in the course of their work. In 1985, the Occupational Safety and Health Administration (OSHA) set a long-term limit of 1 ppm EtO averaged over an 8-h period but decided not to limit short-term exposure. This decision touched off a controversy because workers are often exposed to concentrated bursts of the gas (for example, when the door of a sterilizing machine is opened) and the long-term limit would permit these higher short-term exposures (e.g., up to 480 ppm for 1 min, 48 ppm for 10 min, etc.). The question is this: Is exposure to short bursts of ethylene oxide more hazardous than exposure to the same total dose at a constant low level over a long period? Put another way, Is there a dose rate effect, and if so, how large is it?

Subsequently, OSHA asked the Environmental Mutagen Society (EMS) to study the available findings pertaining to this issue. The EMS committee, of which I was a member, concluded that not enough information was available to assess the importance of dose rate in determining mutational yield. This dilemma prompted me to use a genetic approach to study the issue. I knew from previous results that the dominant-lethal test can quantify the effects of various EtO exposure conditions.

My co-workers and I exposed three groups of male mice to EtO.

Generoso prepares a lens for photographing defects in mouse fetuses.

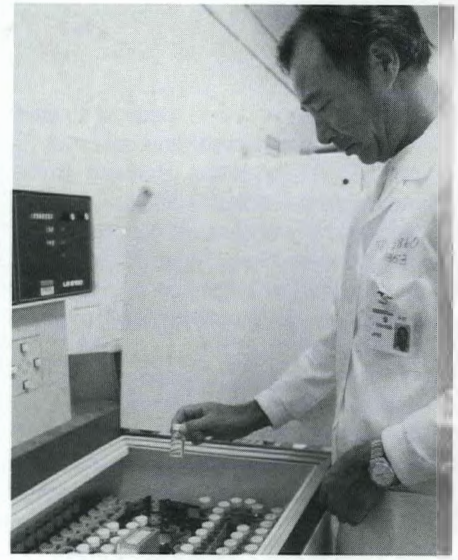
The cumulative dose received by each group was the same (1800 ppm/h). However, three different dose rates were used: 300 ppm for 6 h, 600 ppm for 3 h, and 1200 ppm for 1.5 h. We found that dominant-lethal mutations resulting in deaths among embryos sired by exposed mice was higher in the two groups exposed to higher doses over time. Compared with the group receiving 300 ppm for 6 h, dominant lethals were about three times as high in the group receiving 600 ppm for 3 h and about six times as high in the group receiving 1200 ppm for 1.5 h.

A parallel molecular study by Gary Sega of the Mammalian Genetics and Reproduction Section of the Biology Division also revealed a dose-rate effect on the amount of unscheduled DNA synthesis in spermatids. The spermatid stage does not normally undergo DNA synthesis, but when chemicals bind to DNA, at this stage, the spermatid responds by repairing certain altered sites. By providing the germ cells with radioactive thymidine, Sega

Ruby Valdivia recovers mouse sperm to measure chemical binding after in vivo exposure.

measured the relative amounts of DNA repair synthesis (thus, DNA damage) at various dose rates.

Up to this point, all the ORNL results had been obtained from experiments in which the exposure levels were at much higher concentrations than workers normally encounter in the workplace. The question that remained to be answered was: Do dose-rate effects also exist at low exposure levels? Sega tried to determine whether EtO binds to germ cells at low exposures. Using tritium-labeled EtO, he found that inhalation exposure of male mice to as little as 1 ppm/h of EtO resulted in 6000 to 7000 alkylations (bindings of EtO) for every germ cell. This finding is significant because the total exposure to the mice was well below the daily total exposure allowed under the OSHA guidelines in the absence of a short-term exposure limit. Sega is currently conducting a molecular dosimetry study to determine whether a dose-rate effect on the amount of germ-cell alkylation exists at low exposure levels. This study is necessary because genetic methods are not sensitive enough for use at levels so low as to correspond to the short-burst human exposure. In addition, it will be important to relate endpoints



Isao Yoshikawa prepares to measure the binding of radioactively labeled ethylene oxide to the germ-cell DNA of female mice. The DNA is dissolved in a scintillation fluor, and then radioactivity is measured in the liquid scintillation counter.

such as alkylations to biological effects for them to be useful for risk assessment.

EtO Forms Adducts with Chromosomal DNA and Protein

EtO chromosome breaks that lead to dominant lethality and heritable reciprocal translocations occur because EtO reacts with molecular target sites in the chromosomes. The chromosomes of affected germ cells are composed solely of DNA and the protein called protamine. Sega and his co-workers have been trying to determine which specific reaction products, or adducts, are responsible for chromosome breakage. They found that the extent of EtO binding to protamine is highest in germ-cell stages that also show the highest dominant-lethal response. This finding is significant because it implies that, in addition to DNA, damage to this protamine macromolecule is also important in genetic risk evaluation.

EtO Adduct Data Could Aid Predictions about Cancer Chances

When ethylene oxide is inhaled by a human, how much of the substance—or of the products of its metabolism—actually sticks to DNA? Knowing the answer is important to biomathematicians trying to predict the probability that a person exposed to the gas will contract cancer as a result of the exposure.

The study of the ethylene oxide "adduct" is barely under way at ORNL because of the difficulty of measuring EtO binding on specific DNA sites. However, Gary Sega of the Biology Division (see main article) has been able to measure EtO adducts on mouse DNA. Curtis Travis of the Health and Safety Research Division hopes to develop mathematical models based on data from exposures of test animals to high amounts of the gas. His models assume a linear relationship between the amount of EtO or its metabolite attached to DNA and the probability that the exposed person will develop tumors.

An adduct is a complex formed when a chemical covalently bonds with DNA. The electrostatic forces that allow the chemical to attach to the DNA cause the DNA molecules to bend. As a result, the DNA molecules are more likely to "make mistakes" in replication, mistakes that could lead to cancer.

The prospect of measuring adducts in human blood or tissues has given rise to a hot, new field called molecular epidemiology. The idea is to gauge the probable health effects of exposures to a potentially cancer-causing substance by measuring the fraction of the substance that actually clings to the DNA. The amount of the adduct is believed to be directly proportional to the probability of development of cancer.

Molecular epidemiology faces a couple of problems, however. Direct measurement of adducts is extremely difficult. Radiolabeled monoclonal antibodies that seek out specific adducts have been developed for only a few carcinogenic agents, such as benzo(*a*)pyrene [B(*a*)P]. No such method exists for EtO. In ORNL's Environmental Sciences Division (ESD), Lee Shugart is investigating an alternative approach by studying hemoglobin adducts of B*a*P in fish.

A second problem is that persons exposed to potentially hazardous substances may be reluctant to submit to blood or tissue tests to determine exposures. However, the technique could be used on animals in the area of an industrial plant or waste-disposal facility to relate levels of exposure to toxic substances to probable health effects. Such biomonitoring is now being studied by Barbara Walton of ESD and graduate student Sylvia Talmage.

According to Travis, it may turn out that the relationship between exposures and health effects may not be determined simply by measuring adducts. The relationship, he says, is probably affected by other factors such as how long and where the adduct "sits" on the DNA molecules. Meanwhile, as research on adducts continues and better methods of measuring EtO and other adducts are developed, Travis will work on a mathematical model predicting health effects of EtO. Using the expected new information, he hopes to refine the model for EtO and other adducts that he is studying. With increases in funding from the U.S. Environmental Protection Agency for this work, Travis is finding adducts irresistible if not addictive.—*Carolyn Krause*

Sega and co-workers have quantified the formation of specific DNA adducts in the mouse testis. Using high-performance liquid chromatography, they identified the radioactive peaks resulting from EtO binding to specific sites on guanine, one of the bases found in DNA. In addition, they obtained evidence that EtO may be binding to phosphate groups of the DNA backbone. If left unrepaired, any of these DNA adducts have the potential to cause genetic damage.

Extrapolation from Mouse to Man

The extent of occupational exposure to EtO can be measured either by molecular dosimetry or by monitoring mutational response in certain somatic cells. Human germ cells, on the other hand, are generally not accessible for dosimetric and genetic studies. To bridge the gap between the two types of cells, animal models must be used.

Julian Preston of the Biology Division has been studying the induction and persistence of chromosome aberrations and sister-chromatid exchanges in mouse peripheral lymphocytes following long-term exposure to EtO. His objective is to relate the frequency of chromosomal aberrations in somatic cells to similar alterations in germ cells.

Preston has spent many years in research using radiation and chemical agents that are designed to provide estimates of the genetic risk to humans from the induction of chromosomal alterations in mice. In addition, he has been actively involved with the Ethylene Oxide Industry Council and Chemical Manufacturers' Association as an expert witness at the OSHA hearings on the regulation of EtO (see sidebar on page 18) and as a member of a team of experts that inform these organizations about current EtO research findings and their ramifications for predicting adverse genetic and somatic health effects resulting from EtO exposures.

Yoshikawa shows a DNA preparation he has made from mouse germ cells exposed to radioactively labeled ethylene oxide gas. The DNA will be analyzed for the amount of bound EtO. Looking on are Generoso and Gary Sega.

Gary Sega injects a sample of hydrolyzed DNA into a high-performance liquid chromatography (HPLC) system. The DNA was recovered from mouse germ cells exposed in vivo to labeled ethylene oxide gas. The HPLC system can separate various DNA adducts produced by different chemical mutagens.

Differences among Mouse Strains

Biology Division researchers in the laboratories of Raymond Popp and Gary Sega are studying the differences in sensitivity of various mouse strains to the potential toxic and genetic effects of EtO. Susan Niemann, a University of Tennessee graduate student of Popp's, observed that one mouse strain is markedly more sensitive than most other strains to EtO's toxic effects after long-term repeated exposure. Niemann and Popp concluded from breeding tests that the germ cells of males from this strain also undergo greater damage than do those of other strains, as indicated by increased dominant lethality, reduced fertility, and reduced litter size. They attribute this strain's toxic reaction to EtO to kidney failure, which, they speculate, is caused by a single gene. The biochemical basis of this sensitivity is under investigation.

In Sega's laboratory, Isao Yoshikawa, a visiting research professor from Nagasaki University in Japan, and Dan Brat, an undergraduate research participant from Earlham College in Richmond, Indiana, are studying another aspect of mouse strain differences. Like Niemann and Popp, these investigators also observed strain differences in the toxicity response to EtO; the response in this case, though, was to a single (rather than repeated) exposure to EtO. A dominant-lethal study that I had performed, however, indicated that all the strains had similar responses. Sega's group is investigating whether mouse strains differ in the rate at which EtO binds to various tissues, including the testis and ovary.

The separate studies of Sega and Popp on the genetic and molecular bases for strain differences in mice may be useful in assessing potential differences in human sensitivity.

A New Discovery

The zygotic stage, which covers the period from sperm entry into the egg to the first cleavage division, lasts for almost a day in the mouse. It is characterized by a series of complex developmental changes, including the formation of male and female pronuclei and pronuclear DNA synthesis. The pronuclei in zygotes represent the ultimate stage in male and female gametogenesis (production of mature germ cells) because the respective genetic contributions are not yet united in the egg.

It has long been assumed that exposure of the zygote stage to noxious agents does not produce adverse effects manifested during the fetal stages. The belief was that if the dose is high enough, exposure of the zygote will lead to early death of embryos but leave surviving fetuses free of developmental abnormalities. A new discovery at ORNL is challenging these assumptions.

Recently, I observed that, if previously mated females inhale EtO at about the time the sperm enters the egg or during the early

Ethylene Oxide: The Regulatory Picture

Ethylene oxide is used mainly in industry as a chemical intermediate. The U.S. Environmental Protection Agency regulates its use and discharge by private concerns.

Only about 1% of all EtO consumed in the United States is used as a pesticide to fumigate imported beehives or sterilize medical instruments in hospitals, for example. Regulation of human exposure to the chemical is the responsibility of the U.S. Occupational Safety and Health Administration (OSHA).

According to OSHA's John Martonik, the currently permitted exposure level for workers is 1 part per million EtO averaged over an 8-h period. This standard, based on the belief that risk of cancer is related to cumulative dose, has been challenged in court. In the summer of 1986, the U.S. Circuit Court of Appeals for the District of Columbia ruled that OSHA should have considered the dose-rate effect of EtO in light of recent scientific studies. These studies, particularly those done by Walderico Generoso at ORNL (see main article), suggest that exposure to a 15-min burst of the gas is more hazardous than the gradual release of the same amount during a working day.

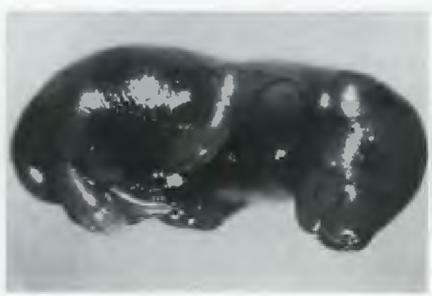
OSHA staff members are now working on a proposal for a short-term limit (e.g., 15 min) on human exposure to EtO. The proposal should be ready for internal OSHA review by February 1987; later in the year, the proposal will be published, a hearing will be held, and a final standard will be established.

Martonik said that Generoso's work called attention to the problem of the dose rate effect and that his results will be used by OSHA as additional justification for the proposed short-term limit.

EPA is also using information generated from Liane Russell's specific-locus test, Gary Sega's testis-alkylation studies, and Generoso's chromosome-aberration work to help it determine the risk of genetic damage in mammals from exposure to EtO. Says EPA's Richard Hill: "Ethylene oxide is an excellent example of a chemical for which enough data exist to allow us to proceed with a full-blown risk assessment."

Absent Lower Jaw

Exposed Brain



Vestigial Eye

Edematous

Examples of developmental anomalies produced in mice when mothers were exposed to ethylene oxide during the zygotic stage of the conceptuses.

pronuclear stage of the zygote, the resulting offspring have a high incidence of varied developmental defects. These effects were absent or minimal for females exposed either within days before mating or when the embryos were in later zygotic stages (during pronuclear DNA synthesis) or had reached the two-cell stage. The remarkably stage-dependent sensitivity and varied nature of the fetal defects found suggest a genetic basis for the response. Subsequently, the induction of congenital defects from exposure of the zygotic stage has been observed by us for three other mutagens (ethyl methanesulfonate, ethylnitrosourea, and mitomycin C).

With respect to induction of varied fetal defects, the zygote is clearly vulnerable to certain chemical mutagens. My group is currently studying the genetic nature of the response. The new finding is expected to have impact on chemical safety evaluation. It raises questions regarding the vulnerability of human zygotes when the mother is exposed to environmental chemicals. The finding suggests that, under certain conditions, women who are exposed to mutagenic chemicals on the day after conceiving may be unwittingly putting their future children at risk.

Genetic Risk of EtO

A definite need exists for a widely accepted strategy and guidelines for carrying out genetic risk assessment for environmental

A mouse zygote at 6 h after mating showing the male (the bigger of the two) and the female pronuclei. Exposure of this early pronuclear stage to ethylene oxide results in congenital defects.

Researchers study the binding of chemical mutagens to mammalian germ cells. They are, from left, Ruby Valdivia, Dan Brat, Isao Yoshikawa, Gary Sega, Waldy Generoso, and his wife, Estela Generoso.

chemical mutagens. The important question is, How effective is the chemical expected to be at various possible human exposure levels? To answer this question, several genetic risk assessment methods have been proposed. The goal, therefore, in using EtO as a model is to produce the set of data needed to be applied to each of the genetic risk assessment methods proposed. This set includes dosimetric, genetic, and cytogenetic data from somatic cells of exposed workers, and from nonmammalian germ-line genetic test systems. However, data on the transmitted genetic effects in mice constitute the gold standard in this exercise. ORNL's Biology Division, which has gathered such data, is thus playing a crucial role in the development of methods and guidelines for the genetic risk assessment of ethylene oxide and other environmental chemical mutagens.

Three ORNL Inventions among Top 100 Technical Achievements

A "smart" sensor that mimics the ability of the human sense of smell to detect a diverse mix of hazardous gases is one of three Oak Ridge National Laboratory inventions named among the top 100 research and development achievements in 1986 by *Research & Development* magazine. The other two achievements are a sophisticated device for measuring very-low-intensity radiation emitted by synchrotron light sources for materials studies and an inexpensive analytical tool for detecting complex mixtures of chemical compounds.

The latest I-R 100 awards to Martin Marietta Energy Systems, Inc., scientists and engineers bring to 55 the total won by Department of Energy facilities since 1967. Winners are selected from among thousands of scientific and engineering achievements on the basis of importance, uniqueness, and usefulness.

The ORNL award-winning developments and inventors are an integrated gas analysis and sensing chip by Robert J. Lauf (Metals and Ceramics Division), Barbara S. Hoffheins and Michael S. Emery (Instrumentation and Controls Division), and Melvin W. Siegel (Carnegie-Mellon University); a multimode ionization detector by Michelle V. Buchanan and Marcus B. Wise (Analytical Chemistry Division); and a soft X-ray emission spectrometer by Tom A. Callcott (University of Tennessee and Health and Safety Research Division), Edward T. Arakawa (Health and Safety Research Division), Ken L. Tsang (University of Tennessee), and David L. Ederer (National Bureau of Standards).

Here are profiles of the three winning achievements.

Integrated gas analysis and sensing (IGAS) chip: Pattern-recognition techniques that mimic the human ability to smell diverse odors are applied in a smart chemical sensor that detects complex mixtures of hazardous gases. The IGAS chip was developed in a collaborative program funded by the Cabot Corporation involving researchers from ORNL and Carnegie-Mellon University.

Conventional single-catalyst tin-oxide gas sensors can achieve high sensitivity but do not selectively detect particular reactive gases. The ORNL sensor combines several catalysts having different properties on a single substrate. When exposed to reactive gases, the IGAS chip catalysts produce multiple electrical signatures that permit a microprocessor to recognize individual gases and measure concentrations.

The integrated gas analysis and sensing (IGAS) chip is an intelligent chemical sensor that mimics the human sense of smell to detect a diverse mix of hazardous gases. The developers include, from left, Michael Emery, Barbara Hoffheins, and Bob Lauf, all from ORNL.

Production of IGAS chips involves advanced thick-film hybrid circuit techniques and special catalytic "inks" that are printed on a substrate and fired at high temperatures. The device has applications in process and environmental monitoring and control and may be used to monitor raw materials and products in food processing, fermentation, and oil refining.

Multimode ionization detector: This instrument is a continuously tunable chromatographic device used to selectively detect compounds in complex mixtures. It combines the characteristics of three separate detectors in one relatively inexpensive device.

Used to detect isomers—one of two or more chemical substances having the same composition and molecular weight, but different structure and properties—the device consists of an electron-capture cell within a variable-pressure vacuum chamber. Depending on the selected chamber pressure, the device can be operated as either a conventional electron-capture detector, argon ionization detector, or tunable selective detector.

ORNL's multimode ionization detector provides isomeric data that can be obtained only by using mass spectrometers that are over 20 times more expensive. The instrument can selectively detect several classes of compounds in the presence of other compounds.

Marcus Wise and Michelle Buchanan of ORNL developed the multimode ionization detector, a continuously tunable chromatographic device for selectively detecting compounds in complex mixtures.

Soft X-ray emission spectrometer: This instrument measures very-low-intensity radiation more than 10,000 times more efficiently than conventional spectrometers—for use in basic materials studies. The device is designed for measuring spectra created by synchrotron radiation sources. Currently, it is being used on a beamline at the National Synchrotron Light Source at Brookhaven National Laboratory. The new spectrometer was developed as part of a collaborative research effort funded by the National Science Foundation.

Several key modifications that enhance light-collection capability enable the new spectrometer to achieve extremely high efficiencies in the study of soft X-ray spectra. These spectra can provide important information about the electronic states of abundant and technologically important light elements. Scientists can now obtain unprecedented measurements of low-level impurities in samples, time-dependent processes on surfaces and alloys, photon-excited spectra from fragile samples, and spatially resolved spectra using scanned microprobe electron beams.

The soft X-ray emission spectrometer measures very-low-intensity radiation more than 10,000 times more efficiently than conventional spectrometers for studies of basic materials. The new spectrometer, designed for measuring spectra created by synchrotron radiation sources, was developed as part of a collaborative research effort funded by the National Science Foundation. The developers are, from left, David Ederer, National Bureau of Standards; Ken Tsang, University of Tennessee; Tom Callcott, UT and ORNL; and (not shown) Ed Arakawa, ORNL.

ORNL Designs Reactor for Space

Oak Ridge National Laboratory engineers have been conducting conceptual design studies of nuclear-power systems for outer space. The space reactor study has been done as part of ORNL's participation in the Strategic Defense Initiative (SDI) Program.

Space platforms designed to carry weapons will need three levels of electrical production: (1) housekeeping power, to maintain basic functions; (2) alert power, to get the platform equipment ready to do battle; and (3) burst power, to meet the electrical demands of lasers, accelerators, and other weapons during the battle encounter. The SP-100 reactor being developed at Hanford Engineering Development Laboratory for the Air Force and the National Aeronautic and Space Administration can provide housekeeping power, but another concept is needed to supply alert and burst power.

To provide the higher levels of power, ORNL proposes a nuclear alkali-metal Rankine power system because of its potential as an efficient, lightweight power plant. John C. Moyers and his colleagues in the Engineering Technology Division and other ORNL divisions have carried out conceptual design studies of reactors cooled by either boiling potassium or liquid lithium. Potassium would be used as the Rankine power-cycle working fluid. The reactor core would consist of metallic-clad rods fueled with uranium nitride pellets.

ORNL researchers have developed a computational model to provide conceptual designs of the reactor and its power-conversion and heat-rejection subsystems and to estimate performance and mass for each of the subsystems and for the complete power system.

Analyses using the model have shown that nuclear alkali-metal Rankine power systems offer reasonable thermal efficiency and system mass. The model has also proven to be a valuable tool for selecting optimum design specifications.

The ORNL reactor concept is one of several types of space power systems being considered by the SDI program. Other concepts include gas-cooled reactors having either open- or closed-cycle Brayton power conversion, liquid-metal-cooled reactors having open-cycle power conversion, thermionic reactors, and chemically fueled systems. SDI will select two or three of the concepts for further development in fiscal 1987. The final selection of a concept will be made in fiscal 1991.

If the mass of the nuclear Rankine-cycle system proposed by ORNL could be decreased, the concept would be even more attractive because it would be lighter and easier to loft into orbit. Such a reduction in mass could be achieved by including an energy-storage device that extracts excess power or waste heat from the system, stores it, and releases it for use when needed (e.g., for burst power—a very high power for a very short time).

Recently, ORNL's Mitch Olszewski found that integrating a flywheel with a nuclear Rankine-cycle system reduces the mass of the primary power system by 25% for a generation time of 500 s. He also found that the heat-rejection system mass could be reduced by 50% if energy storage is used in conjunction with the radiator.

Olszewski has studied a variety of storage technologies, including flywheels, electrochemical batteries, fuel cells, superconducting magnets, and capacitors. He has concluded that the most promising of these near-term storage technologies is the flywheel, but he expects that it eventually will face competition from the battery and fuel cell.

ORNL reactor designers have their eye on the sky, but their concepts are down-to-earth.

ORNL Develops Method To Detect Wear in Motor-Operated Valves

Motor-operated valves (MOVs) are used in nuclear power plant safety systems. Unexpected wear-related failures of the motors or valves have required extensive maintenance commitments and resulted in the loss of operational readiness. To help reduce maintenance costs and ensure that safety systems are ready to respond to reactor emergencies at all times, electric utility companies need a method for monitoring degradation and detecting age-related defects that develop in MOVs. Such a method would allow repair or replacement of components before they become nonfunctional, causing a loss of safety protection.

ORNL experiments using these two motor-operated valves revealed that the electric current supplied to the motor during a valve cycle was useful in detecting and monitoring mechanical load variations in the drive train, which transmits motor power to the valve. The information provided by the motor current can indicate whether components are operating normally or are in need of repair or replacement.

A potentially superior diagnostic method for MOVs has been developed by Dave Eissenberg and Howard Haynes of ORNL's Engineering Technology Division. They have discovered that monitoring the current going through the motor provides useful information about how the motor operators and the valves they drive are functioning.

The motor of an MOV transmits power to the valve through a complex drive train, providing the needed torque to raise or lower the valve stem. ORNL experiments using two large MOVs revealed that the electric current supplied to the motor during a valve cycle was useful for detecting and following many mechanical load variations in the drive train. The motor acts as a transducer by converting significant mechanical load variations of the valve and operator to current variations that may be easily monitored.

Eissenberg and Haynes use a remote nonintrusive current probe to detect the motor-current signature during valve operation. From the signal, they extract four levels of information—mean value for a cycle, gross trends during a cycle, transients, and noise frequency spectra.

Using motor-current signature analysis, the ORNL engineers recently identified a problem in an 8-cm (3-in.) gate valve at a Tennessee Valley Authority (TVA) training center. In response to the ORNL analysis, TVA lubricated the motor operator only at the specific location identified from the analysis. ORNL's subsequent motor-current analysis obtained the expected signature, verifying that the problem was eliminated.

The ORNL technique has identified several types of degradation and many drive-train mechanical load features previously undetectable or requiring intrusive monitoring methods. The ORNL engineers found that the technique can also be used to detect mechanical load features of other electric motor-driven devices, such as vacuum pumps and fans.

Use of the motor current offers several advantages over current diagnostic practices, say the ORNL engineers. Unlike other target variables, motor current can be monitored nonintrusively and remotely; it can be measured during plant power operation; and it can be inexpensively and rapidly measured using conventional electronic equipment.

The motor-current method is superior to accelerometer-based analysis because it detects all load-generated spectra but no spectra from other sources; it requires no access or mechanical attachment to the MOV; and as a transducer, it is linked directly to the load.

The U.S. Nuclear Regulatory Commission (NRC) is particularly interested in the ability of motor-current signatures to characterize transient events, thus providing the information needed to correctly set torque and limit switches for valves. The ORNL method is superior to current measurement techniques because it alone is nonintrusive.

ORNL plans to develop a data base of diagnostic information about laboratory MOVs in which defects are implanted and about commercial nuclear power plant MOVs. A logic for analyzing MOV diagnostics, including criteria for continuing operation, will be developed. And ORNL will make recommendations concerning the use of the new MOV diagnostic tool to the NRC, the sponsor of this development.

The U.S. Department of Energy has prepared a patent application covering aspects of this development, and ORNL is now taking additional steps to transfer the technology to industry. ornl

take a number

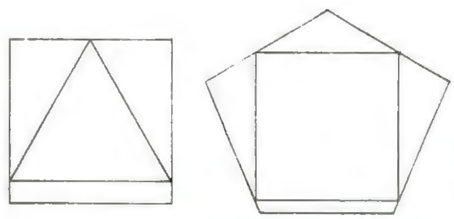
By V. R. R. Uppuluri

Only True for Squares and for Pentagons

In an equilateral triangle, the three sides are equal in length and each angle equals 60°. A square has four equal sides, and each angle equals 90°. As illustrated here, an equilateral triangle can be inscribed in a square—that is, the three vertices of the equilateral triangle lie on the sides of the square.

In a regular pentagon, the five sides are equal and each angle equals 108°. As illustrated here, a square can be inscribed in a regular pentagon.

However, in a regular hexagon (six equal sides, each angle equal to 120°), a regular pentagon cannot be inscribed. In general, an $(n - 1)$-sided regular polygon cannot be inscribed in an n-sided regular polygon for $n \geqslant 6$.



On Irrationals

A number is said to be rational whenever it can be expressed as the ratio of two integers; otherwise, it is said to be irrational. For example, $\sqrt{2}$ is an irrational number.

Rational numbers, when raised to the powers of rational numbers, may give rational numbers. For example, $2^2 = 4$. Irrational numbers, when raised to the powers of irrational numbers, may also give rise to rational numbers. For example, take 2, raise it to power $\sqrt{2}$, take the square root of this result, and raise the result to power $\sqrt{2}$. The final result is 2. Thus, $[\mathit{sqrt}(2^{\sqrt{2}})]^{\sqrt{2}} = 2$.

Take a Number from 1 through 4

David G. Gosslee, an ORNL statistician for more than 25 years, retired in March 1987. In tribute to him, I present this guest article he wrote on some observations he made several years ago:

During a series of traveling lectures, I asked graduate students at six universities to choose a number from 1 through 4. The object of each exercise was to demonstrate that subjective attempts to randomize may fail and that objective procedures are necessary when planning experiments and surveys. A major statistical principle in planning and analyzing experiments and surveys requires that units be selected randomly.

In my surveys, I found that the frequencies with which the number 3 was selected relative to the number of students were 23/59, 16/38, 18/40, 14/31, 10/25, and 17/42. A simple test of randomness, in this case, is to compare the observed percentage of 3's with 25%, the expected percentage if the selection was truly random. This comparison is appropriate as a test of my hypothesis, made before performing the exercises, that an excess of 3's would be selected by each class. The percentages of 3's observed are 39%, 42%, 45%, 45%, 40%, and 40%, while the 95% confidence limits are 34%, 37%, 36%, 38%, 39%, and 36%, respectively. Because the observed percentages are greater than their corresponding limits, I conclude that they are significantly greater than 25% for each of the six classes. The approximate 95% confidence limits were calculated by the formula, $25 + 71.2/\sqrt{N}$, where N is the number of students in the class.

In short, people don't choose among the numbers 1, 2, 3, and 4 in a random manner. This demonstration is one of several showing that persons generally do not select sample units randomly unless some objective method of random selection—rolling a die, for example—is used.

Fran Sharples, an ecologist in ORNL's Environmental Sciences Division, currently works in the Hazardous Waste Remedial Actions Program. A native of Brooklyn, New York, she came to ORNL in 1978 after earning her Ph.D. degree in zoology. She has worked in ORNL's Program Planning and Analysis Office, where she managed the Laboratory's institutional planning process. In 1981 she went to Washington, D.C., for a few months as an American Association for the Advancement of Science (AAAS)/Environmental Protection Agency Environmental Science and Engineering Fellow, where she did some of the earliest work on the environmental implications of genetic engineering. In June 1983 she testified on this topic before two subcommittees of the Committee on Science and Technology of the U.S. House of Representatives. In 1984, she became a member of the Recombinant DNA Advisory Committee of the National Institutes of Health. In 1984–1985 she spent a year in Washington as a AAAS Congressional Science and Engineering Fellow. Although she was appointed to the Committee because of her expertise on the environmental aspects of recombinant DNA, she has participated in Committee activities concerning all major aspects of genetic engineering technology. Human gene therapy is one of the many subjects to which the

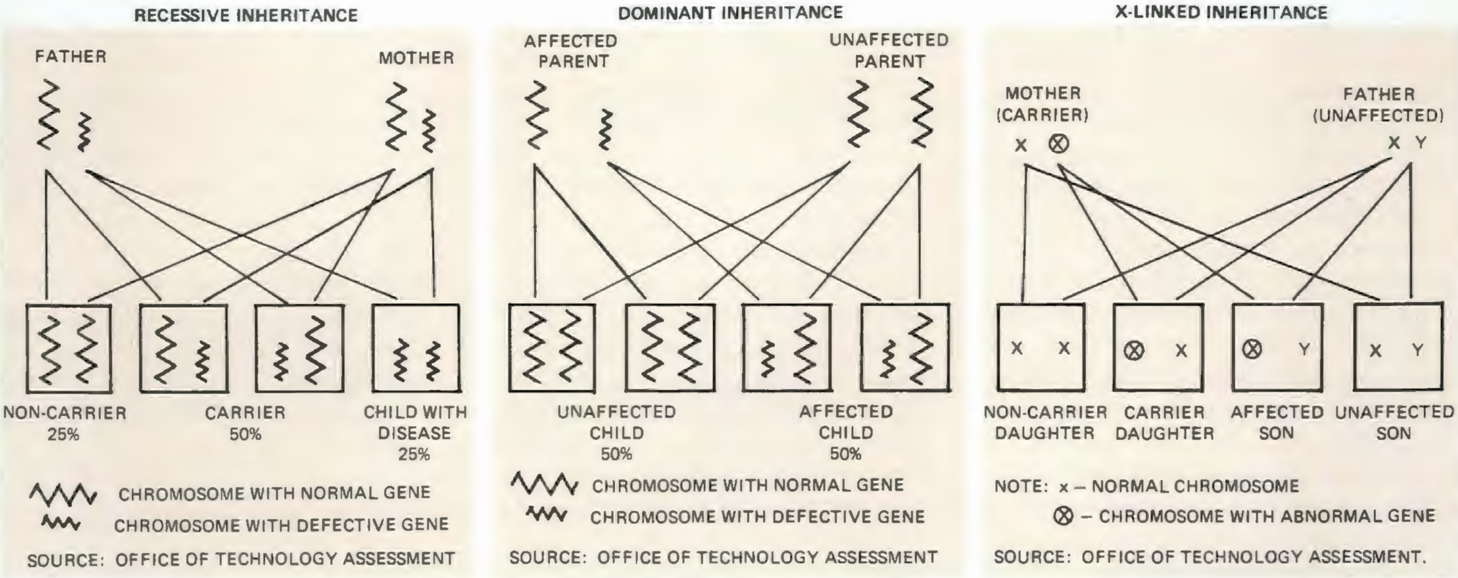
Committee has devoted considerable attention over the last two to three years. Because she found the topic so fascinating, she has contributed this article to the Review *to share some of what she has learned.*

Human Gene Therapy:
A Look at a Cutting Edge of Biomedical Science

By FRANCES SHARPLES

Early in this century, Sir Archibald Garrod, a brilliant British physician, observed that the urine of patients suffering from the disease alkaptonuria contained large quantities of homogentisic acid, an unusual biochemical product that was entirely absent from normal human urine. He also noted that these patients' siblings frequently had the disease, although their parents and more distant relatives did not, and that the parents of such patients exhibited high incidences of marriage among close relatives.

Garrod developed the hypothesis that this and other diseases that produce unusual biochemical products represent "inborn errors of metabolism." Such errors affect



Humans have 23 pairs of chromosomes; one pair (the X and Y) is the sex-determining pair, and the rest are nonsex chromosomes, or autosomes. A recessive mutation must be carried on both members of a chromosome pair to be completely expressed. Individuals having only a single copy of a recessive defect on one member of an autosomal pair usually do not manifest clinical signs of the defect, but can serve as carriers to pass the defect on to their offspring. About 25% of children from pairings between carriers of recessive traits are expected to inherit two copies and express the mutation. A dominant defect, however, need be present on only one autosome of a pair to be expressed. Children of affected parents and carrier parents are therefore statistically more likely to express the defect as well. X-linked traits are more apt to be expressed in men, who have only one X chromosome, than in women, who must have a copy of the defect on each of their X chromosomes for expression.

enzymes, which are the protein catalysts that govern the body's biochemical reactions. A defect in, or the absence of, a particular enzyme could block a biochemical pathway, resulting in the accumulation of abnormal metabolites, just as Garrod had observed in his patients. He subsequently learned from Gregory Bateson, one of the great early geneticists, that the particular kind of familial distribution Garrod had observed for diseases like alkaptonuria fit the pattern for recessive traits described by Gregor Mendel's recently rediscovered laws of inheritance. This relationship suggested that the cause of alkaptonuria is a genetic defect and that this defect must have something to do with a missing enzyme.

Modern Picture of Genetic Disorders

Half a century later, Garrod's hypothesis was directly confirmed when it was demonstrated that the activity of the enzyme for degrading homogentisic acid was unmeasurable in patients having alkaptonuria. The relationship between altered or missing enzymes and mutations in genes is now well defined. The human genetic complement, or genome, is estimated to contain between 50,000 and 100,000 genes, and approximately 1400 single-gene-determined (monogenic) human diseases are known to exist. The biochemical basis has been defined for only about 250 of these, but of those defined about 170 involve abnormalities in enzymes. Defects may also occur in a wide variety of other protein types, including transport proteins, hormones, structural proteins, and coagulation factors.

In addition, genetic disorders can also result from chromosomal abnormalities (e.g., Down's syndrome) that may involve the gain or loss of a chromosome or chromosome piece. Finally, many disease conditions and birth defects that appear to "run in families"

Gene therapy—implanting appropriate genes in cells to correct genetic disorders—is being considered for widespread use in humans with inherited diseases. The author, who is a member of a national committee that considers the technical, ethical, and social implications of this biomedical technology, describes the technical merits and problems of human gene therapy and current recommendations on its future use.

(e.g., hypertension, diabetes, peptic ulcers, cleft lip and palate, spina bifida, and congenital heart disease) do not fit monogenic inheritance patterns; this group of disorders is thought to represent "multifactorial" or "polygenic" diseases in which genes at independent loci may interact with other genes and with environmental factors in a cumulative manner. The precise number of genes that may be responsible for such polygenic traits is, however, unknown, and these disorders rarely manifest themselves in an all-or-none fashion as do monogenic traits. Not surprisingly, the monogenic disorders are the easiest genetic diseases to understand in detail and the ones most likely to yield to successful treatment.

Monogenic disorders show three different types of inheritance patterns (see three figures): (1) autosomal dominant; (2) autosomal recessive; and (3) X-linked. The term dominant implies that a mutation can be expressed even when an individual has only a single "dose" of that mutation—that is, it occurs on only one chromosome of a matched pair. (In higher organisms, all chromosomes come in pairs except the X and Y, or "sex" chromosomes. Each member of a pair of nonsex chromosomes, or autosomes, carries genes for the same functions, but may differ in having slightly variant forms, or alleles, for any particular gene.) In general, the biochemical nature of most dominant monogenic disorders is not well understood.

For clinical expression of recessive autosomal defects, it is necessary for an individual to have the defective allele on both members of a chromosome pair. This produces a typical inheritance pattern in which the parents of the affected individual are normal because each one has only one copy of the defective gene, but siblings, both male and female, have a 1 in 4 chance of also being affected by the disease. In contrast, X-linked monogenic disorders are rarely encountered in female patients. In humans, males have an X and a Y chromosome, while females have a pair of X's. Thus, an important defect in one X-linked gene in a male is usually displayed as a full-blown disorder regardless of whether the mutation involves a recessive or dominant trait in females. The disorder appears because no set of genes exists on the Y chromosome to balance the effects of one defective copy on the X chromosome. Only X-linked dominant traits, however, are expressed in females affected by a single dose. Females who express an X-linked recessive disorder are rare because the probability of a woman inheriting a defective X chromosome from both her father and her mother is low, particularly because many X-linked disorders result in a much reduced chance of successful reproduction in an affected man.

Sickle-cell anemia, familial hypercholesterolemia, Huntington's disease, cystic fibrosis, hemophilia, and many others are prominent examples of single-gene defects. Most of the other monogenic disorders are extremely rare. Only 1 in 10,000 male children, or 200 new cases each year, are affected by Lesch-Nyhan syndrome in the United States. Only 40 to 50 cases of adenosine deaminase deficiency have been reported worldwide, and only nine patients in six families are known to suffer from purine nucleoside phosphorylase deficiency. Taken singly, this extreme rarity makes these conditions "orphan" diseases. But collectively, monogenic disorders may affect 1% to 2% of newborns and may account directly for more than 5% of all pediatric hospital admissions. The overall population frequency of monogenic disorders is about 10 per 1000 live births, of which about 7 in 1000 are autosomal dominants; 2.5 in 1000, autosomal recessives; and 0.4 in 1000, X-linked conditions. Thus, these disorders are by no means medically or socially insignificant. In addition, however, several of these rare disorders may also become better known as a focus of the new area of biomedical science called gene therapy.

Prospects for Human Gene Therapy

Gene therapy involves isolating a gene, putting it into cells where it can function, and ensuring that it functions in a way that does not harm the patient. The term gene therapy could, in fact, be used to describe several different procedures:

- gene insertion, in which a new version of a gene is introduced into a cell;
- gene modification, in which a gene is altered in place; and
- gene surgery, in which a defective gene is excised and is replaced by its normal counterpart.

Current prospects for gene therapy do not include either gene modification or gene surgery because these actions are much more complex than merely adding genes to cells. In addition, it is not now scientifically possible to perform gene therapy for chromosomal disorders, even in experimental animals. Therefore, the definition of gene therapy used here will refer strictly to the insertion of a normal gene into an organism to correct a genetic defect. This feat, which has already been performed successfully in fruit flies and mice, has been made possible largely by rapid advances in recombinant DNA technology. The questions are, How soon, and under what circumstances, will gene therapy be available for humans?

For now, the answer to the first question can only be "in the near future." Investigators in the human gene therapy field believe that it could occur over the next couple of years. What will the first trials in human gene therapy attempt to accomplish? Early clinical experiments will probably have the following characteristics:

• *They will be performed on the somatic cells of patients.* Somatic cells make up all body tissues except the reproductive, or germ, cells. Because only modifications of germ cells are heritable, an alteration in the genetic material of somatic cells would not be passed on to the next generation. Although it may someday be feasible to modify the human germ line, both technical and ethical problems of large proportions make this avenue of medical research much more unlikely than gene therapy on somatic cells. Despite the extensive public debate over the wisdom of tampering with the human genome, civil, religious, scientific, and medical groups have so far agreed that gene therapy on somatic cells for specific diseases is appropriate and is largely perceived as merely an extension of current therapeutic practice.

• *They will focus on cell types that can be readily removed from the body, manipulated in vitro, cultured, and replaced into the body.* Only bone marrow and skin cells are currently suitable for such use. The first attempts at gene therapy will almost certainly focus on correction of defects in cells that originate in the bone marrow because these lend themselves best to removal, manipulation, and replacement. In fact, bone marrow transplantation is already the major therapy of choice for the correction of biochemical defects with genetic causes. About 90% of patients who receive bone marrow transplants for this purpose achieve a successful cure. Why bother then with the high-tech unknowns of gene therapy? The reason is that suitable bone marrow donors are found for only about 30% of ill individuals who might be cured by transplants. Thus, because the vast majority of these individuals cannot be treated in this way, they must wait for the development of gene-therapy techniques.

• *They will be performed to allay symptoms caused by a defect in a single gene whose normal counterpart has been cloned.* Obviously, a defect cannot be corrected by the insertion of a normal gene if the identity and location of the gene on the human chromosome is unknown.

• *They will focus on genes that are responsible for the production of proteins whose expression in the body need not be carefully controlled and that have a simple "always on" type of regulation.* In some cases, the amount of a protein produced in the body is very important. For example, a defect in the gene for growth hormone results in dwarfism in humans. A comparable defective growth hormone gene in a mouse strain known as *Little* produces dwarf mice. The first genetic "cure" reported in a mammal consisted of inserting a rat growth hormone gene into the cells of these mice in such a way that the gene was expressed—translated into protein—at a high level. The gene was not, however, appropriately controlled. Too much growth hormone was produced, and gigantism resulted (i.e., the treated mice grew to one-and-a-half times normal size). Obviously, it would not be appropriate to risk such an outcome in a human patient. Such an undesirable result can be avoided only if the normal feedback controls regulating the expression of the inserted DNA are well understood.

Similarly, clinical investigators initially thought that hemoglobin disorders such as sickle-cell anemia and thalassemia would be the first to be treated through gene therapy. These diseases are probably the most common monogenic disorders throughout the world. They are also the best studied and defined of all human genetic disorders. The defects in hemoglobin molecules have been pinpointed, and the affected cells arise in readily accessible bone marrow. But the control of expression of the genes for the various forms of hemoglobin is very complex. Embryonic, fetal, and adult hemoglobins are produced in the body in very carefully timed and controlled ways. In addition, the alpha and beta chains that make up a single adult hemoglobin molecule are always maintained in a 1-to-1 ratio in the body, despite the fact that the alpha and beta gene loci are found on different chromosomes. The extreme complexity of the globin gene system will therefore require much more study before gene therapy for the related hemoglobin disorders can be safely attempted in humans.

• *Gene therapy will be considered only if no alternative treatment available to individual patients is preferable.* Any new medical technology has associated uncertainties and risks, and human gene therapy is no exception. It is unfortunate but true, however, that, for many victims of genetic disorders, no medical alternatives exist for the treatment of debilitating, and even life-threatening, conditions. For these patients, even a low probability of success using a new therapy outweighs the uncertainties and risks of the treatment.

The Most Likely Candidates

The three genes that are the most likely candidates for the first attempts at gene therapy are those that code for the production of the enzymes purine nucleoside phosphorylase (PNP), adenosine deaminase (ADA), and hypoxanthine-guanine phosphoribosyl transferase (HPRT). In all three cases, the defects mainly involve bone marrow and the normal gene counterparts can be cloned. The individuals affected by the disorders associated with defects in these genes are primarily children.

The absence of PNP results in a severe immunodeficiency disease. Affected patients lack the "cellular" immunity that normal individuals derive from the class of lymphocytes known as T-cells. They are thus predisposed to recurrent and persistent infections. Such individuals do, however, have normal, or near normal, B-cell function. (The B-cells produce immunoglobulins). The T-cell dysfunction that occurs in PNP deficiency disease is thought to be the result of the toxic buildup of the enzyme's undegraded substrate.

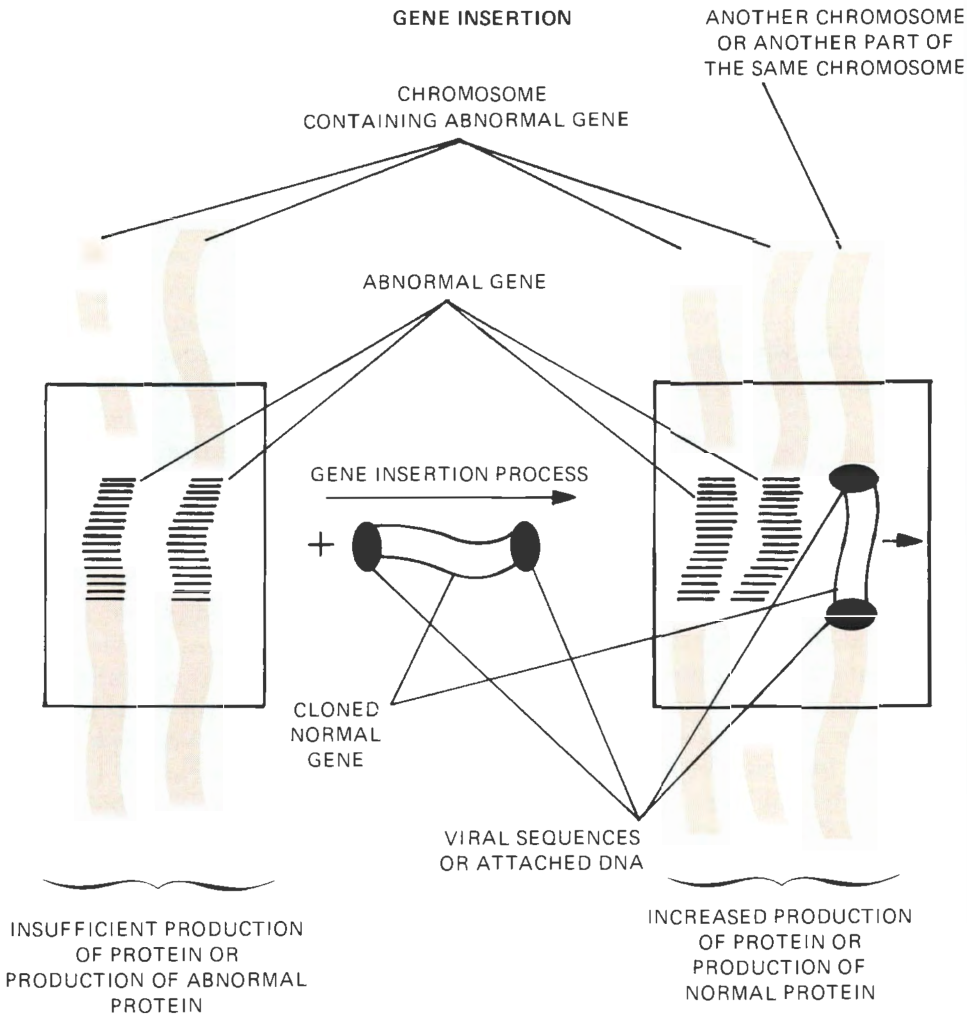
A defective gene for ADA also results in an immune deficiency disease, but in this case both the T-cells and the B-cells are lacking. This condition, referred to as severe combined immunodeficiency disease (SCID), is therefore much more severe than PNP deficiency. Unless heroic special measures are taken, as in the case of David the "Bubble Boy" (see photograph on page 31), children born with SCID usually die from overwhelming infections before they are two years old. The biochemical mechanism for pathogenesis in SCID also seems to be related to an accumulation of metabolites that are toxic to T- and B-cells.

Without HPRT, the purine metabolic pathway that should convert hypoxanthine to inosinic acid is short-circuited, and one of the results is excessive production of uric acid. In patients with only partial HPRT deficiency, this uric acid buildup causes a severe form of gout. In cases of virtually complete HPRT deficiency, however, the result is the much more severe Lesch-Nyhan syndrome. The most striking feature of this syndrome is compulsive self-destructive behavior. Between the ages of 2 and 16, children with Lesch-Nyhan disease begin to mutilate themselves, biting fingers, lips, and the insides of their mouths. The self-mutilating urge is so strong that many patients must spend their lives under constant restraint or have their teeth removed to avoid infliction of serious damage. These children also often exhibit

Examples of diseases for which gene therapy might be considered

1. Protocols for human gene therapy in somatic cells expected in next several years
   - immunodeficiency caused by adenosine deaminase or purine nucleoside phosphorylase deficiencies (ADA or PNP deficiencies)
   - Lesch-Nyhan syndrome (complete hypoxanthineguanine phosphoribosyl transferase deficiency)
   - urea-cycle defects caused by deficiencies of arginosuccinate synthetase (citrullinemia) or ornithine carbamoyl transferase (OCT, also known as ornithine transcarbamylase)
2. Might be attempted in foreseeable future
   - phenylketonuria (as improvement on current dietary treatment)
   - familial hypercholesterolemia
   - defects of the urea cycle other than citrullinemia and OCT deficiency, for example, arginemia (arginase deficiency)
   - mucopolysaccharidoses and other defined metabolic defects
     - — Gaucher disease (some forms) metachromatic leukodystrophy (arylsulfatase B deficiency type with little brain involvement)
     - — Hunter syndrome (enzyme detectable in normal blood)
     - — branched-chain ketoaciduria (severe grades)
3. Farther off because protein expression may require regulation
   - hemoglobinopathies
     - — sickle cell disease
     - — alpha and beta thalassemia
   - hormone-production defects
4. Farther off because gene product may be easily available for administration (diminishing the need for gene therapy)
   - growth-hormone deficiency; some other hormone production defects
   - hemophilias
5. Unlikely unless new discoveries provide clues on how to approach gene therapy (some may require germ-line therapy because of access to tissue sites or immunologic problems with gene product)
   - Tay-Sachs disease and other metabolic defects that primarily affect the brain
   - cystic fibrosis
   - type 1A growth hormone deficiency
   - most diseases inherited in dominant pattern (e.g., Huntington disease, Marfan syndrome, achondroplasia, etc.)
6. May not be applicable
   - chromosomal disorders such as Down syndrome
   - environmental and multigenic disorders
     - — hypertension
     - — diabetes

[a]Cloned human-gene available.
Source: Office of Technology Assessment



SOURCE: OFFICE OF TECHNOLOGY ASSESSMENT

In the human gene therapy process, an abnormality in a pair of chromosomes is corrected by the addition of a cloned segment encoding the normal gene. Insertion of the cloned segment will produce the missing gene product.

extremely aggressive behavior towards others and are characteristically mentally retarded. Just how the biochemical defect translates into the bizarre neurological features of Lesch-Nyhan is unknown.

How It's Done

The goal of gene therapy is to transfer copies of a normal gene into cultured human cells that can then be reimplanted. These cells should then proliferate, forming a population of normal cells (e.g., lymphocytes) in the patient's body.

The usual first step in gene therapy is to identify both the abnormal gene and its normal counterpart. Then the normal gene must be cloned—that is, made in multiple copies. Cloning involves recombining the gene of interest with the DNA of a lower organism, usually a bacterium, using special enzymes that cut and then reseal the strands of DNA in their new location. Then as the bacteria reproduce, more and more copies of the inserted gene are made. These copies must then be retrieved from the bacteria, cut away from the unwanted bacterial DNA, and purified. They must then be prepared for the method by which the gene will be inserted into human cells.

The DNA containing the normal human gene can be inserted into human cells in several ways: using viruses as vectors, or vehicles, to carry the DNA into the cell; physically injecting it; using chemicals to induce the cells to take up the DNA; or fusing cells with membranes containing the DNA. Currently, the most promising method appears to be the use of viral vectors. In this case, the human genetic information for insertion must be combined with the genetic material of the virus, which is then allowed to infect bone marrow cells. A special group of viruses, called retroviruses, seem, at this time, to offer the most advantages as a gene delivery system. Retroviruses are somewhat unusual in that their genetic material is RNA, not DNA. When the virus infects a target cell, it makes a reverse transcription of its RNA into DNA which then integrates into the DNA of the host cell. A retrovirus that has not been tampered with in the laboratory is then able to reproduce itself using the host's own apparatus for replication.

The advantages of using a retroviral vector are that (1) a fairly large percentage of cells in a bone-marrow culture can be infected, (2) large numbers of cells can be infected simultaneously, and (3) the human DNA for insertion is more likely to integrate into the DNA of the bone marrow cells as a single copy. Physical and chemical methods often result in multiple copies of the normal gene being inserted, which is not desirable.

Problems of Gene Therapy

There are, however, a few problems that must still be overcome before human gene therapy is attempted. To produce any benefit, the inserted normal human gene obviously must be expressed after transfer to the patient's bone marrow cells. Investigators have experienced difficulty both in achieving gene expression in cell cultures and after replacement of the bone marrow back into the bodies of experimental animals. As of the spring of 1986, however, several investigators had shown that they can "cure" ADA-deficient lymphocytes in culture by transfer of the normal ADA gene. The ADA gene had also been successfully transferred and expressed when reimplanted into monkeys, although the level of expression achieved was probably too low to produce any clinical improvement were such an implant to occur in a human patient.

Besides the problem of gene expression, practitioners of human gene therapy must also combat the problem of potential health hazards. For example, in animals it is known that insertion of viral regulatory sequences near an oncogene, a gene that stimulates cell growth, can activate the oncogene, causing cancer. It is not yet known whether this unwanted effect might occur in implanted human bone marrow cells, but investigators are attempting to steer clear of this potential problem by designing vectors that would lose their regulatory sequences during integration. Another safety problem being addressed pertains to the vectors for gene therapy; vectors are being designed that cannot be transmitted further once they have entered a target cell, thus ensuring that nontarget cells are not also at risk for infection. At least one group of investigators, however, has discovered the unexpected presence of a "helper" virus that could be transmitted to the experimental animal with the vector, allowing the vector to continue to reproduce and infect cells other than the target ones. At this point, investigators in the gene therapy field are hopeful that these technical problems will be overcome soon so that the first clinical trials can begin.

RAC's Role

Another aspect of the application of human gene therapy somewhat outside the realm of technical concerns is the need for constant consideration of ethical and social implications. It is here, especially, that the activities of the National Institutes of Health's (NIH's) Recombinant DNA Advisory Committee (RAC), of which I am a member, have been most significant.

In 1982, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research issued a report entitled "Splicing Life: The Social and Ethical Issues of Genetic Engineering with Human Beings." This report found that continuing oversight of the field of genetic engineering was desirable and recommended several ways of doing it. One of these was to build upon the successful history of the RAC, modifying its composition to include the necessary additional areas of expertise. Subsequently, the conclusion was reached that no other national body comparable to the RAC existed to deal with the ethical and social issues of genetic engineering. The RAC, therefore, accepted this new oversight responsibility by establishing a Working Group on Human Gene Therapy. The Working Group is composed of 15 members whose areas of expertise include laboratory science, clinical medicine, ethics, law, and public policy. It also has an expert consultant on retroviruses.

Over the last several years, the Working Group has endeavored to create a procedure for detailed review and evaluation of human gene therapy protocols. The results of the Working Group's efforts appear in a document called "Points to Consider in the Design and Submission of Human Somatic Cell Gene Therapy Protocols," which has been published in the *Federal Register*. The outline for the procedure presented in the "Points to Consider" requires a review of each protocol that is consistent with the procedures set out in the NIH *Guidelines for Research Involving Recombinant DNA Molecules* for other recombinant DNA experiments that require RAC review. As part of the new process, both the Working Group itself and the full RAC must approve a proposed experiment. Protocols must follow the U.S. Department of Health and Human Services' *Regulations for Research Involving Human Subjects.*

In addition, investigators must provide information sufficient to satisfy the Working Group and RAC that a number of issues have received adequate attention. First, investigators must demonstrate that the technical aspects of the research protocol are valid and appropriate and that the risks and benefits of the therapy have been carefully considered. Second, the selection of subjects is expected to be conducted with fairness and equity to ensure that all suitable patients have equal access to therapy. Third, investigators must document their efforts to achieve informed consent of patients and their relatives. The issue of

Members of the Recombinant DNA Advisory Committee of the National Institutes of Health convened in September 1986. Standing fourth from right in the back row is the author.

informed consent for human gene therapy is complicated both because of the complexity of the technology to be used and because the first subjects are likely to be pediatric patients. Fourth, an explanation of measures that will be used to protect the privacy and confidentiality of patients to avoid the "circus-like" atmosphere that often surrounds medical firsts is required. Finally, investigators are asked to reveal the steps they will take to ensure that other researchers, clinicians, and the public are accurately informed about progress, problems, or other areas of public concern.

Thus, an overall framework is in place to provide safeguards to protect the safety, rights, and privacy of the first human gene therapy patients. It should not be long now before the first proposals for actually attempting this therapy are received. As a member of RAC, I have greatly enjoyed participating in making decisions concerning the implementation of techniques that will undoubtedly make medical history. ornl

David, the "Bubble Boy" who lived all his life in a germ-free bubble in Texas, suffered from severe combined immunodeficiency disease, the result of a single-gene defect. He had virtually no immune system. He died at the age of 12 in 1984.

Tommy Wright is a member of the Statistics Group of the Mathematical Sciences Section of ORNL's Engineering Physics and Mathematics Division. A native of Birmingham, Alabama, he received degrees in mathematics from Knoxville College (B.S., 1969) and the University of Tennessee (M.S., 1970). After serving for four years on the faculty at Knoxville College, he returned to graduate school and received a Ph.D. degree in statistics from Ohio State University in 1977. He taught mathematics two more years at Knoxville College and then, in 1979, joined the Computer Sciences Division of Union Carbide Corporation's Nuclear Division (now the Computing and Telecommunications Division of Martin Marietta Energy Systems, Inc.) in Oak Ridge. In 1980 he was an invited discussant at the U.S. Census Bureau's Conference on the Census Undercount. In 1981–1982 he served on a National Academy of Sciences panel that reviewed the statistical program of the U.S. Bureau of Mines. In 1982 he chaired the organizing committee for the Small Conference on the Improvement of the Quality of Data Collected by Data Collection Systems held in Oak Ridge; he also edited the conference proceedings, which were published by Academic Press. During parts of 1984 and 1985, he was visiting associate professor of statistics at the University of Tennessee. Wright's research interests center on problems related to sampling from a finite population and the general design of sample surveys for various studies. He has assisted in the design and review of sample surveys for several federal agencies. Currently he is an associate editor of *The American Journal of Mathematical and Management Sciences*, a founding member of the Board of Directors of the Tennessee Mathematics and Computer Sciences Foundation, and a member of the American Statistical Association's Advisory Committee to the U.S. Census Bureau.

Survey Sampling:

A Useful Tool for Scientific Investigation

By TOMMY WRIGHT

"...all scientific observation, whether statistical or not, is based on sampling."

—F. F. Stephan

Readers of daily newspapers and weekly news magazines and viewers of television news programs are bombarded with data in the form of numbers, charts, and tables. We see that a Gallup Poll has determined that a certain proportion of the U.S. population feels a certain way about a particular issue. Nielsen's Ratings tell the approximate number of people who watched television in a previous week and the proportion that watched a particular program. Advertisers claim that one product is preferred over another. The TV networks make numerical projections to predict the outcome of national and local elections before the polls close—much to the dismay of losing candidates. Forest personnel can estimate efficiently the number of deer inhabiting a certain land area without actually counting them all. Reliable estimates of world grain production

Scientists at ORNL have used statistics and survey sampling to ensure accuracy in their research results. Examples include determining the proportion of transuranic wastes in waste mixtures, estimating the average number of units per U.S. nuclear power plant, validating energy data, and estimating the size of fish populations at various sites. The author presents a primer on conducting a sample survey.

can be made before harvest by use of satellite data. Much of this numerical information is made possible by an application of statistics called survey sampling.

Indeed the teacher who gives an examination is testing on a sample of that which was taught; the performance on the sample (test) is used to make an inference about all that the student has learned. Each day our senses take many unconscious and informal sample surveys that form the foundation for many of our inferences and actions.

The classical approach to survey sampling assumes that a *finite population* exists and that the units (*U*) in the population can usually be represented as $U_1, U_2, \ldots, U_N$. For example, Oak Ridge National Laboratory employees form a finite population of approximately 5000 people. Often information on some *quantitative characteristic(s)* of a given population is desired. For example, ORNL's management may want to know what percentage of ORNL employees come to work in carpools. This proportion is a quantitative characteristic of the ORNL employee population.

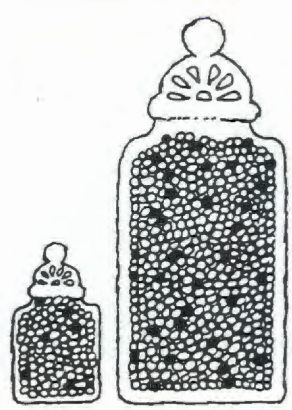
Another example at ORNL of an interesting population and its characteristic was a collection of 1800 drums stored at the Transuranic Waste Assay Facility. These drums contained contaminated rags, gloves, and other materials that had been used in the handling of radioactive substances. It was important to know the mean concentration of radioactive substances in each drum to determine whether they should be disposed of as low-level wastes or held for later disposal at a federal facility for transuranic wastes.

It is traditional to assume that the finite population and characteristic(s) of interest are fixed (constant). Generally, the values of a given population's quantitative characteristics are unknown but ideally could be known if all members of the population were interviewed or measured and if accurate responses could be obtained. Because of time, expense, and other important concerns, one can usually look at only a *sample* (relatively small portion) of the population. *Statistics* (characteristics of the sample) are computed using information collected from the small, manageable sample and are used to make *estimates* (technical guesses) concerning the value of the unknown population characteristic(s).

In practice, however, the job is not so easy. Some later examples will show that the finiteness of the population is not always as clearly defined as in the examples just mentioned. Also, the estimates that are reported for the unknown characteristic(s) depend upon the sample chosen. Although we desire a sample that will provide good estimates of the unknown characteristics, it is certainly conceivable that the sample information could lead to a very incorrect estimate for the value of the population characteristic. Thus, we need to know about *variability* and the chance, or *probability*, of obtaining a particular sample value; these determinations allow us to say how good a particular estimation procedure is.

Because the results of applying sampling techniques affect all of our lives and because many ORNL staff members make formal (and informal) use of these techniques to varying degrees, I will discuss classical survey sampling and demonstrate its wide use. In this way, I will illustrate why some mathematical statisticians study the theoretical properties of various sampling and estimation plans and seek to introduce new ones better suited for existing and new situations.

It is (not) ridiculous to think that one can determine anything about a population of 230 million people, or even 1 million people, from a sample of a few thousand. The number of people in the country bears almost no relationship to the size of the sample required to reach a prescribed precision. Consider a jar of black and white beans. If the beans are really mixed, a cupful would determine pretty accurately the proportion of beans that are black. The cupful would still suffice and would give the same precision for a whole carload of beans, provided the beans in the carload were thoroughly mixed. The problem lies in mixing the beans. The statistician accomplishes mixing by the use of random numbers.—*W. E. Deming.*



What Is a Sample Survey?

According to the American Statistical Association booklet *What is a Survey?*, a sample survey is a "method of gathering information from a number of individuals (units), a 'sample,' in order to learn something about the larger (finite) population from which the sample has been drawn . . . Surveys come in many different forms and have a wide variety of purposes, but they do have certain characteristics in common. Unlike a census, we gather information from only a small sample of people (or farms, businesses, or other units, depending on the purpose of the study). In a bona fide survey, the sample is not selected haphazardly or only from persons who volunteer to participate. It is scientifically chosen so that each individual in the population has a known chance (probability) of selection. In this way, the results can be reliably projected to the larger (population) . . . The survey's intent is not to describe the particular individuals who by chance are part of the sample, but to obtain a statistical profile of the population."

Documentation of early applications of formal survey sampling techniques is sketchy. As F. F. Stephan noted in 1948 in a journal article on the history of sampling, " . . . all scientific observation, whether statistical or not, is based on sampling . . . The earliest examples of sampling procedures are to be found in certain very ordinary human activities. The common practice of taking a small part or portion for testing to determine the characteristics of the whole precedes recorded history and is one of the roots from which sampling methodology stems . . ."

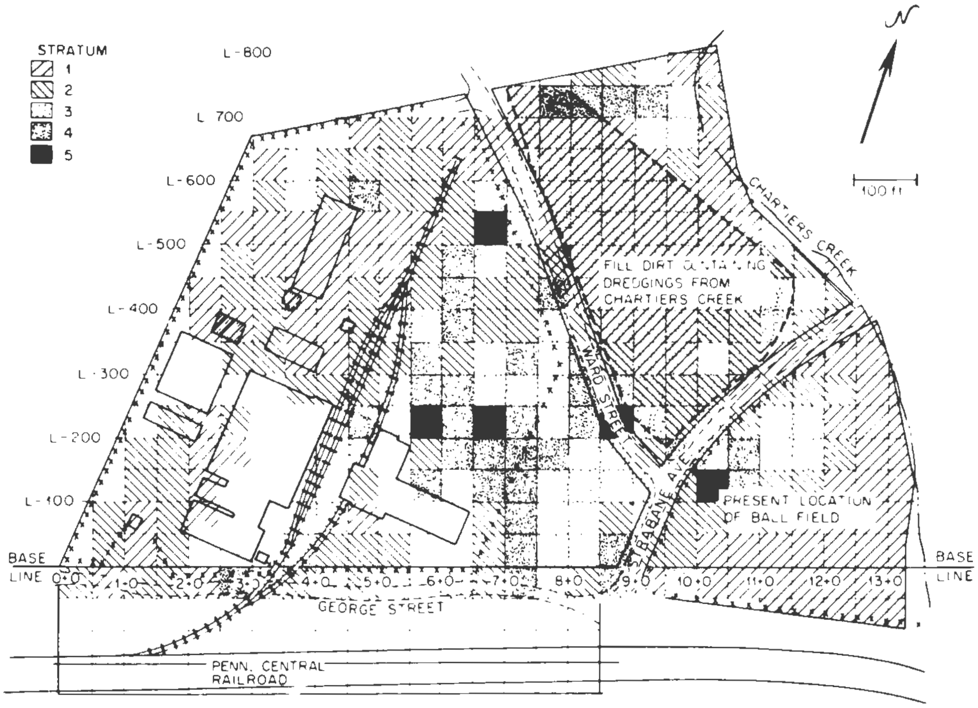
When factors such as time and costs dictated that a complete census was not possible, sampling was the alternative. In many cases, the early uses of sampling were examples of nonprobability sampling, the selection of a sample without use of a known probability scheme. Examples of nonprobability samples given by W. G. Cochran in his world-renowned book Sampling Techniques include: (1) samples that are restricted to sections of the population that are readily accessible, (2) samples that are selected haphazardly, (3) samples that are chosen because they are believed to "represent" the larger population, and (4) samples that consist of volunteers. Experience has shown that nonprobability sampling can lead to bias in the selection of units and, hence, in the estimates. On the other hand, probability sampling makes use of the laws of probability in the selection of the sample and in the construction of efficient estimators. Unlike nonprobability sampling, probability sampling provides an objective means for judging the accuracy of an estimate.

In 1913 A. L. Bowley used systematic selection of every 20th household of working-class people in Reading, England, and computed measures of goodness (standard deviations) of the estimates. Bowley is often considered the first to use probability and statistical theory to guide the design and interpretation of results from sample surveys.

Historically, the application of sampling techniques has had its ups and downs largely because of misconceptions about sampling. At the heart of these misconceptions is the persistent belief that contacting all units rather than only a sample provides the only reliable information about a given finite population. Although in some cases a census would be better than a sample, numerous examples show that the reverse would hold. Although modern, large-capacity, high-speed computers can handle huge amounts of census data more efficiently, the quality of the computer output is no greater than the quality of the input. Many data collectors realize that, because large data sets can contain a large number of errors, it is often preferable to use resources to develop a well-designed, small-scale sample survey for collecting high-quality data rather than to increase the size of the sample by taking a census.

One skeptic about sampling who became a believer is a federal official who contracted work to several ORNL researchers. In 1980, the Energy Information Administration (EIA) of the Department of Energy (DOE) asked ORNL (through the Data Validation Project headed by Andrew S. Loebl, Energy Division) to determine the average number of electricity-generating units per operating power plant (nuclear, coal-fired, oil-fired, hydroelectric, etc.) in the United States.

A Federal Power Commission Data Collection System at the time received monthly reports from 3558 plants, but no one at EIA or ORNL knew how to obtain the number of generating units except by contacting all 3558 managers. But time and resources were not available to take a census. Thus, a carefully designed probability sample of 79 plants was selected, and information was obtained over the telephone. Using the results of the survey, ORNL researchers estimated that the average number of units per plant for the power plant population was roughly 3.51 and that the estimated standard deviation of the estimator was 1.2. Under some assumptions, this means that we might say that there is a 95% confidence that the true average number of units per plant



Canonsburg Industrial Park Site stratification. ORNL researchers proposed to the Nuclear Regulatory Commission that use of a sample survey could be helpful in determining the number of hot spots in a facility during cleanup or decommissioning. In the above schematic of Canonsburg Industrial Park, a site, such as the former Vitro Rare Metals Plant, would be partitioned into square blocks. The number of blocks on the site, denoted by N, is known. The ith block on the site is called a hot spot if the maximum number of μR/h for the ith block exceeds some fixed number, say B.

is between 1.16 and 5.86 [i.e., 3.51 ± 1.96 (1.2)].

By using sampling rather than taking a census, the ORNL researchers completed the entire project in less than a month. Though the project monitor in EIA thought our estimate was low and expressed some strong reservations about using sampling, he accepted our estimate and used it as the basis for decision making. Several months later, we learned from this same project monitor that someone had given him a report that enabled him to determine the number of units for each power plant in the United States. Using this information, he calculated the average number of units to be approximately 3.35 units per plant, very close to the ORNL estimate of 3.51. As a result of this experience, he said he became a believer in sampling techniques—gratifying news for the members of that survey team.

Who Does Sample Surveys?

Sample surveys are performed throughout the world by a variety of individuals, groups, organizations, and governments. Other than opinion polls, most surveys are used for specific administrative or commercial purposes. The most common subject areas for surveys include the environmental sciences, natural resources, agricultural production, health and epidemiology, distributive trade, animal populations, housing, demography, employment and unemployment, consumer expenditures, industry, transportation, marketing, food consumption, energy use, education, and mineral availability. In addition to numerous small-scale surveys, huge surveys in these areas are supported regularly by the federal government (also local and state) and private industry; they form the foundation for many of the data bases that support decisions made by government and business and that guide and buttress scientific research.

Sampling at ORNL

Though the application of sampling techniques historically has been focused on human populations, applications to other types of populations are numerous. Here is a sample of the uses of sampling and survey techniques at ORNL.

- *Surveys for validating data collected by EIA censuses and sample surveys.* Populations of interest to DOE include oil and gas fields having proven reserves in the United States; U.S. coal fields; electric power plants; producers, sellers (including refiners), resellers, and retailers of various types of fuels; transporters and storers of crude oil and petroleum products; buildings; manufacturers of boilers; and corporations. ORNL has used various sampling and survey techniques to determine how reliable these data are.
- *A plan for estimating the probability of not detecting hot spots when sampling a site that has been declared free of radioactive materials.* When a licensee informs the appropriate federal agency—Nuclear Regulatory Commission (NRC), Environmental Protection Agency (EPA), or DOE—that it has declared its site clear of radioactive materials, the agency usually requests a radiological survey to verify that the site is indeed clean or safe. An example of such a site is the former Vitro Rare Metals Plant in Canonsburg, Pennsylvania, where ORNL researchers conducted a radiological survey. Their goal was to identify all hot spots and to eliminate them from the site. This identification could be done by carefully checking each block of the

partitioned site, but such a complete survey would be expensive and time-consuming. The use of sampling techniques is an alternative in the decommissioning of sites that offers reduced cost, greater speed, greater scope, and greater accuracy. However, if sampling is to be used, a method is needed to ensure an accurate estimate of the number of hot spots (H) because only a fraction of the site is surveyed. Such a method must address the possibility of missing hot spots in the unsampled areas. A potential exists also for missing hot spots in the sampled areas, especially in the case of weak gamma emitters in the soil or for radiation sources attenuated by shielding. A probability model for a finite population, which makes use of prior information on the possible values of H, is one approach to the problem of measuring the risk or probability of missing hot spots. A preliminary probability model has been proposed by ORNL for consideration in a joint technical report of ORNL and the NRC.

• *A plan for sampling drums to measure average radioactivity levels before temporary storage in the Transuranic Waste Retrievable Storage Facility at ORNL and ultimate disposal at the Waste Isolation Pilot Plant in New Mexico.* Because of limited space, a continuing need exists to appropriately dispose of the ORNL transuranic waste stored below ground in 208-L (55-gal) drums within weather-resistant structures. Waste containing less than 100 nCi/g of transuranic elements can be removed from the current inventory and disposed of as low-level wastes, whereas waste containing greater than 100 nCi/g transuranics must continue to be held in retrievable storage. To make the measurements needed to determine which drums can be buried, Los Alamos National Laboratory developed a transuranic Neutron Interrogation Assay System (NIAS). NIAS provides information much faster than the currently used technique of gamma-ray spectroscopy. At ORNL, a validation study was planned to determine the ability of the NIAS to make adequate measurements. A sampling plan was proposed to test the validity of the measurements from the new system by sampling the finite population of approximately 1800 waste drums and comparing the estimates made by the two detection methods. The sampling plan provides an approach for estimating the proportion of agreement and other parameters that will form the basis for the validation of the new system.

The transuranic Neutron Interrogation Assay System developed at Los Alamos National Laboratory is so sensitive that it can detect 1 mg of fissile material in a transuranic (TRU) waste mixture filling a 208-L (55-gal) drum. It is capable of performing rapid, quantitative assays of wastes and scraps having a low fissile content that are contained in high- or low-density matrices. A computer operates the entire system. Here Don Coffey, ORNL technician, enters TRU waste assay data into a log book.

• *A redesign of the EIA-9A National Sample Survey.* EIA collects information on the volume and prices of liquid fuel sold and who does the buying and selling. A sample of sellers is required to report this data to EIA by filling out questionnaires. In 1982 EIA asked ORNL's Energy Division to redesign its national sample survey for Form EIA-9A, Monthly No. 2 Distillate Price Monitoring Report (now Form EIA-782B, Monthly No. 2 Distillate Sales Report). In this survey, data on the volumes and prices of No. 2 Distillate Fuel Oil and No. 2 Diesel Fuel sold to residences, industrial users, commercial users, and resellers are collected. Respondents (approximately 1865 companies) include refiners, retailers, resellers, and retailer/resellers. Form EIA-9A provided data for estimating the monthly average prices of No. 2 Distillate Fuel Oil and No. 2 Diesel Fuel sold at state and DOE regional levels and the national level.

EIA wanted to renew the sample so that it could shift the reporting burden to other members in the population who were not in

Operating a fork lift, Coffey loads a TRU waste drum onto a drum-loading platform where its waste contents will be measured by the Neutron Interrogation Assay System.

Coffey loads a TRU waste drum into the Neutron Interrogation Assay System. Part of this system consists of a gamma-ray drum scanner, which can detect and measure gamma-ray-emitting isotopes in 208-L (55-gal) drums filled with low-to-medium-density wastes such as rags, towels, rubber gloves, and similar material.

the sample at that time and to account for changes in the population such as changes in company size (some big ones became small, and some small companies grew through mergers). One of the major goals of the redesign was to use probability to substitute a new sample of respondents for at least 50% of the smaller companies who were within 5 months of completing their EIA reporting requirement. Planning focused on selecting the new sample of respondents from companies that were already reporting to EIA on a related form (Form EIA-172).

As a result of involvement with this survey, How Tsao (now with Eastman Kodak Company) and I were able to prove directly that a 1951 closed-form sampling technique, which is used by several federal statistical agencies to maximize the probability of retaining respondents in repeated surveys, is but one of the infinitely many solutions offered by a linear programming approach. This observation helped us to realize that linear programming can be used for the opposite problem: decreasing the probability of retaining respondents. The final sampling plan successfully replaced a major portion of the sample.

• *Use of sampling by members of ORNL's Environmental Sciences Division to estimate the size of fish populations at various sites.* ORNL environmental scientists studying fish populations used the classical capture-recapture technique, one of several methods employed by the U.S. Bureau of the Census to help estimate the number of people missed by the 1980 Census. Basically, this procedure entails drawing an assumed simple random sample from a finite population (usually wildlife) of interest, tagging each animal sampled, and returning the tagged animals to the population. At a later date, another assumed simple random sample is selected from the same population, and the number of tagged animals is observed. (I say "assumed simple random sample" because the theory often assumes this, but in practice evidence shows that the act of tagging affects the way that animals mix. Adjusted sampling techniques and estimation procedures are needed to account for nonrandom mixing of animal populations.) This information forms the basis for an estimate of the unknown size of the population.

• *In a report in* Science *(1984, vol. 224), C. F. Baes and S. B. McLaughlin of the Environmental Sciences Division demonstrated the use of tree sampling to study metal concentrations in annual growth rings from short-leaf pine trees in the Great Smoky Mountains National Park.* They note that by studying tree rings, one can construct records of climate, document heavy-metal pollution, study the relationship between tree growth and air pollution, and examine the relationship between growth and acid rain.

• *Periodic sampling of grass, soil, air, water, and raw milk by the Department of Environmental*

The Phases of a Survey

How is a sample survey conducted? The task can be broken down into several phases.

• **Original study idea.** If you are an investigator who wishes to collect data on some population, you may want to conduct a sample survey. Future choices about your investigation may be based on your careful analysis of the sample data.

• **Formal statement of objectives.** Once you decide to conduct a sample survey, state its general and specific purposes. Check with all persons involved to be sure you know what is needed, and write statements of objectives in clear language before the sample is selected.

• **Identification of target population.** State precisely which units in the population are of interest. For example, if the survey is being conducted on students at a large university, be sure which students are to be studied. You should determine whether to include part-time students, graduate students, graduating students, students on probation, or exchange students.

• **Frame construction.** In the simplest case, a *frame* lists the units in the target population and often includes *auxiliary information* on each unit. This auxiliary information can be of great value in designing an efficient survey. The frame is used for selecting the sample according to the specified rules of probability. You should be careful to ensure that the frame closely matches the target population.

• **Preliminary operational plan.** The preliminary operational plan spells out how the survey will be executed, who will do what, and when it will be done. This plan includes the collection of the data, the summary and analyses of the data, and inferences to be made from analyses of the data.

• **Questionnaire preparation.** The *questionnaire* is the instrument by which the data will be collected from each sample unit. It may vary from a piece of paper with questions and places for written responses to a hand-held computer that asks questions on a tape and records oral responses. In general the questionnaire should be brief and complete. A request for too much information is likely to decrease the chance of eliciting a complete response from a sample unit, while a request for too little information is likely to limit the usefulness of the survey's results. Each question should be clearly worded to minimize any misunderstanding so that all sample units will have uniform understanding of what is being asked. Ask for information that the sample units can provide.

• **Interviewer training.** An interviewer is any person or thing that accepts the response(s) from a sample unit and reports them to the experimenter (the person in charge of the survey) for processing and analysis. Interviewers include persons who receive completed questionnaires by mail, individuals who ask questions over the telephone, experimenters who make measurements on nonhumans as well as humans, and persons who administer questionnaires face-to-face with the sample units. Interviewers who ask questions directly of persons in the sample should be trained not to influence the subjects' responses.

• **Preliminary sampling plan.** The preliminary sampling plan gives the initial plans on all parameters to be estimated and how the sample will be selected from the frame, the estimators to be used in constructing estimates of the unknown parameters, the estimators of sampling error, and required minimum sample sizes. The sampling plan may also contain some plans for exploratory data analysis, which gives the experimenter an opportunity to check some of the initial assumptions about the population that may have influenced the choice of sampling plan as well as to check for potential sources of nonsampling error.

• **The pilot survey.** The *pilot survey* is an actual execution of the entire process (see figure on this page) but on a relatively small scale. Its purpose is to go through all of the previously outlined steps, including the selection and measurement of a relatively small sample to identify problems and make improvements before executing the actual survey. Specifically the pilot survey can be used to (1) check the accuracy of auxiliary data in the frame, (2) improve questions on the questionnaire, (3) obtain information that might be needed to determine the required sample sizes, and (4) improve the information needed to complete sampling and estimation procedures.

• **Final comprehensive sample survey design.** You should be sure that the sample selection procedure will yield the needed data to support your planned data analysis and the final report.

• **Quality control of the data.** Components of data quality include

Management in ORNL's Environmental and Occupational Safety Division. Sampling is done to determine the environmental effects of ORNL operations on the Oak Ridge Reservation and to ensure that ORNL complies with all environmental regulations.

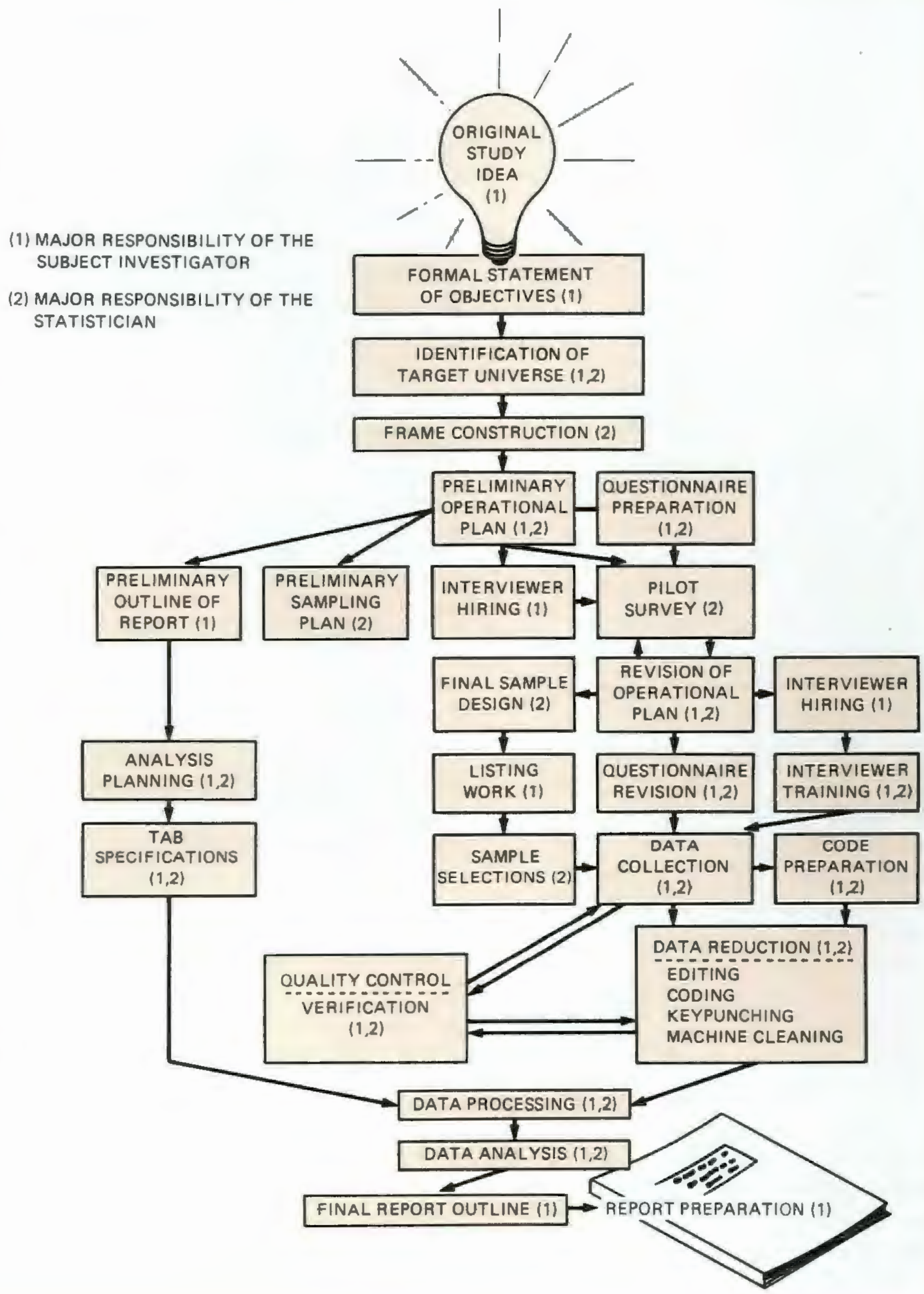
In addition to other applications of sampling at ORNL, sampling is also used by the Y-12 Plant, the Oak Ridge Gaseous Diffusion Plant, and the Martin Marietta Energy Systems internal auditors.

How To Conduct a Sample Survey

Anyone interested in conducting a survey for the first time will find useful advice in *A Sampler on Sampling* (1978) by W. Williams. The book makes clear that sampling involves more than the mere determination of a sample size and the calculation of an average or two. Of course, some sample surveys will not require all of the indicated tasks (see figure below) while other surveys may

accuracy, precision, reliability, timeliness, usefulness, stability, internal consistency, and credibility. Practical experience in dealing with different types of data shows that they can contain gross errors. These errors, if left uncorrected, directly affect analyses and decisions based on the data. Faulty decisions and inappropriate actions could result in a loss of credibility of the data collection system. The question of data quality assessment is indeed a complex one without any complete answers. You should be concerned about the quality of data in the phases *before* and *during* the actual collection as well as *after*.

Many things can go wrong in the execution of a survey. Some of the more commonly occurring problems that should be avoided include
(1) discovering at the end of the survey that no one recalls the purpose of it or that important questions were not asked, (2) being unable to find a good list (frame) of the units in the population from which to select (using probability) the sample, (3) receiving no response from some of the sample units,
(4) being unable to estimate biases and tell how good the data are,
(5) selecting a sampling plan that does not support the survey's objectives,
(6) failing to execute a pilot survey to improve the actual survey, and
(7) failing to give adequate consideration to the determination of the overall sample size. The only way to avoid or minimize these problems is to plan carefully.



require other tasks. We learn from experience that planning for each task (e.g., data collection and analysis) must be done before the sample is selected and the questionnaires are completed (see sidebar).

Sampling Plan and Estimation Procedure

In this section we focus on the topics that draw the attention of most mathematical statisticians interested in sampling—the theory behind the method for selection of the sample and the method of estimation. To illustrate the various considerations, assume a finite population of four units {a, b, c, d}. With each unit in the population is associated a pair of numbers (X, Y). Let the pairs be (2, 1), (3, 2), (8, 7), and (9, 8), respectively, for a, b, c, and d. The X value of each unit is assumed to be known before any sampling is done, and the Y values are assumed to be unknown. A plot of these points shows that they are highly linearly correlated (i.e., they fall on a straight line).

Suppose that an experimenter wants to know the unknown value of the average of the Y-values in the population, denoted as $\overline{Y}$. Constraints permit the selection of only two units for the sample. How should probability be used to select the sample, and how should $\overline{Y}$ be estimated using the sample data? The answer to these questions is obtainable because most of the possible samples that give an estimate close to the true value of $\overline{Y}$ should have high probability of selection. Consider three strategies.

Strategy I: Simple random sampling and sample mean estimator of $\overline{Y}$. The first column of Table A shows the six possible samples of size two. If two units are to be selected at random, then each possible sample has the same probability of selection as indicated in column two of Table A. If the sample mean $\overline{y}_{SM}$ of the sample values in the observed sample is the estimator, then the possible values of $\overline{y}_{SM}$ are given in column three of Table A. Thus, if the sample *bd* is selected, $\overline{Y}$ is estimated by $\overline{y}_{SM} = 5.0$.

Strategy II: Simple random sampling and ratio estimator of $\overline{Y}$. Assume the same sampling plan as under Strategy I. However, note that Strategy I makes no use of the known X values. If the X values are highly correlated with the unknown Y values, as in this example, effective use of the X values can be made. Here, use of the X values can affect the method of estimation by employing, for example, the ratio estimator $\overline{y}_R$, which is equal to the average of all X values times the sum of the Y values in the sample divided by the sum of the X values in the sample. Thus, if the sample *bd* is selected, we would estimate $\overline{Y}$ by

$$\overline{y}_R = \left(\frac{2+3+8+9}{4} \right) \frac{(2+8)}{(3+9)} \approx 4.58 .$$

The other possible values of the estimator $\overline{y}_R$ are given in column four of Table A.

Before continuing with Strategy III, a comparison of Strategies I and II is instructive. Because the true value of $\overline{Y}$ in this example is 4.5, each possible sample gives a value of $\overline{y}_R$, which is as close (actually closer, in four cases) as $\overline{y}_{SM}$ to $\overline{Y}$. Indeed $\overline{y}_R$ has smaller sampling variability than $\overline{y}_{SM}$, and Strategy II is preferred over Strategy I. The smaller sampling variability of $\overline{y}_R$ compared with $\overline{y}_{SM}$ can be shown mathematically to occur in general in simple random sampling when an X variable available is highly correlated with the unknown variable Y.

Strategy III: Stratified random sampling and weighted mean estimator of $\overline{Y}$. In this sampling plan, we begin by grouping a and b together in stratum 1 and then c and d together in stratum 2. Why? The known X values of a and b (and c and d) are close, so the same might hold for the unknown Y values because X and Y are (assumed) highly correlated. If one unit is selected at random from a and b in stratum 1 and (independently) another unit is selected at random from c and d in stratum 2, then the process of selecting the combined sample of two units is called stratified random sampling. The four possible stratified random samples in this case are given in column one of Table B with their probabilities of selection given in column two. Note that $w_1 = 2/4$ of the population is in stratum 1 and $w_2 = 2/4$ of the population is in stratum 2. To give the weighted estimator $\overline{y}_{ST}$, multiply the sample mean of the sample from stratum 1 by 2/4 and add this product to the product of

Table A. Two Estimators under Simple Random Sampling

Sample	P(Sample)	$\overline{y}_{SM}$	$\overline{y}_R$
ab	1/6	1.5	3.3
ac	1/6	4.0	4.4
ad	1/6	4.5	4.5
bc	1/6	4.5	4.5
bd	1/6	5.0	≈ 4.58
cd	1/6	7.5	≈ 4.85

the sample mean of the sample from stratum 2 and 2/4. The possible values of $\overline{y}_{ST}$ are given in column three of Table B.
In this case, because $w_1 = w_2$ and only one unit is selected from each stratum, $\overline{y}_{ST}$ can be computed in the same way as $\overline{y}_{SM}$.

The gain from stratification by grouping like units together before sampling is clearly seen by comparing column three of Table A with column three of Table B. In this example, stratification clearly reduces the sampling variability of the estimator by eliminating the possibility of selecting the worst samples *ab* and *cd*, which give respective estimates $\overline{y}_{SM} = 1.5$ and 7.5—the farthest estimates from the true value $\overline{Y} = 4.5$.

It is clear that Strategies II and III are each superior to Strategy I. However, many seem inclined to use Strategy I in practice, although Strategies II and III are often possible with relatively little extra effort. In fact, the value of Strategy I is quite limited and almost never used by persons engaged in well-designed simple or multipurpose sampling investigations. As many different sampling strategies and estimation procedures exist as do real numbers between 0 and 1; many exist where samples need not be selected with equal probability. Here we focused on only two sampling plans and three estimators of one characteristic, $\overline{Y}$. For a given problem, the mathematical statistician is challenged to select a strategy (using mathematical models) that will yield estimators that are (on the average) as close to the unknown truth as possible.

Concluding Remarks

Huge data collection agencies, such as the EIA and the U.S. Bureau of the Census, have no easy task collecting, processing, analyzing, and providing timely and useful data. They need the help of statisticians to do applied and theoretical research on topics such as (1) minimizing nonresponse and deciding how to adjust the data for nonresponse; (2) estimating errors (particularly sampling errors) in complex national sample surveys; (3) adjusting estimates when the list (sampling frame) from which the sample is selected is incomplete; (4) making good estimates for small subsections (e.g., city) of the population from good estimates for the overall population (e.g., nation); (5) keeping the identity of certain respondents confidential despite the need to publish detailed data; (6) matching data from two or more data sets; and (7) improving overall data quality. These problems intensify when demands for data increase, operating budgets decrease or remain constant, research personnel are lured away by private industry, and the pool of research candidates in sampling and survey methodology continues to be extremely small.

Much of the classical sampling theory developed largely during the first part of the 20th century

underlies today's practice of sampling. The driving force in theory and practice has been "... that the choice of estimator should be directed by considerations involving the sampling design, for example, that the estimator should be unbiased or have a small (sampling) error under the given (sampling) design ...," according to Cassel, Sarndal, and Wretman in their 1977 book *Foundations of Inferences in Survey Sampling* (Wiley Publishers). Much of this thinking stems from Jerzy Neyman's significant 1934 paper, which (among other things) points to a need to select samples using randomization (probability) as opposed to purposive or nonrandomized (nonprobability) sampling. However, over the last two or three decades, some interest has focused on other criteria, including the highly controversial one suggesting that inferences from survey data can be independent of the sampling design. One implication of this idea is that it encourages nonprobability sampling, which is in direct conflict with current practice. The introduction of new criteria has prompted a critical review of the foundations of sampling theory.

As the debates and research continue on competing theories and practices, the application of survey sampling methodology remains an important tool in the collection and careful analysis of information at ORNL and all over the world.

Table B. The Results Under Stratified Random Sampling

Sample	*P*(Sample)	$\overline{y}_{ST}$
ac	(½)(½)= ¼	4.0
ad	(½)(½)= ¼	4.5
bc	(½)(½)= ¼	4.5
bd	(½)(½)= ¼	5.0

Scientists at ORNL helped develop neutron-activation analysis, which has been used for 50 years to identify elements in materials. They have contributed their expertise to evaluating materials suitable for this type of analysis, to determining relative concentrations of uranium in the ground and environment, and to advising manufacturers of computermemory materials. ORNL scientists are now preparing to use the expanded Neutron Activation Analysis Laboratory at the High Flux Isotope Reactor.

Frank Dyer operates remote manipulators in the HFIR neutron activation analysis laboratory.

Nuclear Sleuthing at ORNL:

A New Look at Neutron Activation Analysis

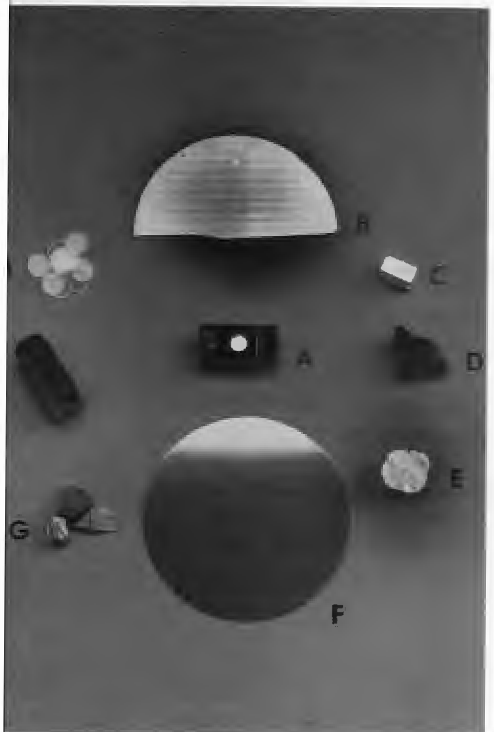
By CAROLYN KRAUSE

A 50-year-old analytical technique, once the rage in the world of crime detectives, is now being used to solve high-tech problems. Although it was praised by comic strip character Dick Tracy 15 years ago, the technique, which uses a nuclear reactor, is no longer the darling of the press. Today neutron activation analysis (NAA) is hardly mentioned in the news media, largely because it is now used only infrequently in solving crimes.

However, nuclear sleuthing still flourishes. NAA is practiced at more than 100 nuclear reactors throughout the world, including about 70 research reactors in North America. Today at Oak Ridge National Laboratory, where early work on the development of NAA was performed, a new $600,000 addition to the Neutron Activation Analysis Laboratory in the High Flux Isotope Reactor (HFIR) is being readied for operation. The facility will be used partly to advance the development of high technology.

The design of the new NAA facility at ORNL may allow for more cost-effective analyses of the uranium content of semiconducting materials that store information in computers. The results of these analyses are helping vendors to develop processes for making materials that have only very low levels of radioactive impurities. The computer-memory-chip industry will not purchase semiconducting materials having unacceptably high levels of uranium because the radioactivity from decay products can alter the information in memory chips, causing "soft" errors. Thus, the data obtained at memories. ORNL is vital for the vendors of materials used in computer

NAA has long been a technical tradition at ORNL. It was first performed at the Laboratory at the old Graphite Reactor; in fact, the



Computer-memory components evaluated in ORNL's electronic materials analysis program: (A) electronically programmable ultraviolet-erasable read-only memory (EPROM) circuit similar to memory chips analyzed at ORNL (integrated-circuit chip can be seen through the window); (B) half of a wafer showing fabricated integrated-circuit chips; (C) high-purity aluminum used for evaporated-metal films (for conductor elements) in integrated circuits; (D) potting material used to form housing of integrated circuits; (E) silicon dioxide from which silicon wafers are made; (F) polished silicon wafer; (G) silicon crystals; (H) container (rabbit) made of high-purity graphite in which samples are irradiated in nuclear reactors; (I) polished high-purity quartz disk (Supersil I) used to record fission tracks during neutron irradiations.

Graphite Reactor was the first nuclear reactor used in the country for performing NAA. The first American textbook on NAA was written at ORNL in 1963 and published a year later. Few people realize that NAA at ORNL was used to analyze evidence related to the 1961-62 French-connection heroin case (subject of an award-winning movie) and the 1963 assassination of President Kennedy. In addition, ORNL radiochemists rendered opinions in federal court on whether NAA evidence should be accepted in two well-publicized murder trials in the late 1960s (see following article). ORNL also developed one of about a half dozen important computer programs used over the years for interpreting NAA results to identify and quantify elements in materials.

From 1975 through 1979, NAA was used extensively for a U.S. Department of Energy (DOE) effort called the National Uranium Resources Evaluation (NURE) program. The purpose of the NURE program was to sample water and soil throughout the United States for uranium (a nuclear power plant fuel) in an attempt to map the distribution of uranium. Part of the project involved use of NAA to measure the concentrations of uranium in the collected samples. ORNL personnel handled almost 100,000 samples.

In the past few years ORNL has been using NAA for environmental analyses. In support of DOE's Formerly Utilized Sites Remedial Action Program (FUSRAP), Juel Emery's Radioanalytical Group in the Analytical Chemistry Division has been measuring uranium-235 and uranium-238 in soil samples from ORNL, the Y-12 Plant, and other FUSRAP sites (e.g., those in New Jersey, Albany and Niagara Falls, New York, and St. Louis). FUSRAP sites are contaminated with waste uranium discharged by old Manhattan Project facilities and by radiopharmaceutical manufacturers.

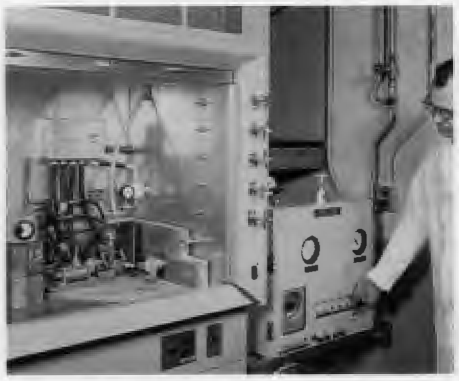
In 1986 DOE compiled a report on the major research efforts funded by its Office of Basic Energy Sciences that have had important impacts on society. Of the 28 chemistry efforts cited, three were credited to ORNL. They are resin-bead isotope ratio mass spectrometry for nuclear safeguards, computerized crystallography, and major developments in NAA.

ORNL researchers over the years involved in NAA research have been George Boyd, George Leddicotte (deceased), William S. Lyon, Richard L. Hahn, Enzo Ricci, J. E. Strain, Lamont C. Bate (deceased), Juel F. Emery, Frank Dyer, and Larry Robinson. For their work, Hahn and Ricci received the American Nuclear Society's Radiation Industry Award in 1977, and in 1981 Lyon became the fifth American scientist to win the George Hevesy Medal, an international honor conferred by the *Journal of Radioanalytical Chemistry*.

NAA Contributions

NAA is a sensitive, versatile, nondestructive analytical tool that uses nuclear particles and their energy. In this technique, a sample of an unknown material is first irradiated, or activated, with neutrons, usually from nuclear reactors. Target atoms bombarded with neutrons absorb some of them and become heavier, unstable radioactive species that quickly disintegrate by emitting high-energy electromagnetic radiations called gamma rays. By measuring the intensities and energies of these gamma rays using a high-resolution gamma spectrometer, scientists obtain a gamma spectrum that they use to determine the identity and concentration of trace elements in the original, nonradioactive sample. (Charged-particle activation analysis—activation with ions instead of neutrons—is also a very useful technique based on the same principle.)

Ed Strain examines data from a 200-channel, vacuum-tube analyzer, which acquired gamma spectra for NAA until 1964. The same type analyzer was used in the Kennedy assassination probe carried out at the Laboratory (see following article).



Juel Emery checks the rabbit tube control panel in preparation for a neutron activation analysis measurement.

Enzo Ricci and Dyer check on neutron activation analysis work in a hot cell.

Gamma spectra from analyzed materials are compared by computer with known spectra for the elements, or "nuclear fingerprints." GAMANAL and MONSTR, two of the most important computer programs used over the years for this purpose, were developed at two DOE facilities—Lawrence Livermore National Laboratory and ORNL, respectively.

The first NAA experiment was carried out 50 years ago. In 1936, four years after the discovery of the neutron, George Hevesy, the Nobel prize-winning Hungarian, working with Hilde Levi in Copenhagen, Denmark, bombarded impure yttrium with neutrons from a small source to activate and measure a trace quantity of the contaminant dysprosium. However, really practical NAA came into existence only after World War II with the advent of nuclear reactors.

Over the years, the popular appeal of NAA has been its use in convicting some persons suspected of committing crimes (see following article). NAA can match bits of material left behind at the scene of a crime to a suspect (e.g., paint particles embedded in the body of a victim of a hit-and-run car accident) or it can identify minute traces of substances that the suspect has carried away from the scene (e.g., specks of dirt from the site where the victim was found).

NAA can also identify art forgeries. By comparing the gamma spectrum of a tiny speck of paint removed from a "great work of art" with the spectrum of pigments available when the work was alleged to have been done, NAA experts can often determine whether the art work is real or fake.

Archeologists have employed NAA to match the elemental composition of clay deposits with finished ceramic products. Using this information, they have identified ancient pottery manufacturing sites and deduced ancient routes of commerce without destroying ancient artifacts.

Hair analysis by NAA has contributed not only to solving crimes but also to knowledge about historical figures. For example, scientists using NAA found an unusual amount of arsenic in relics of hair from Napoleon of France and King Eric XIV of Sweden, suggesting that both could have died from poisoning. Because NAA is a nondestructive technique, the hairs that were analyzed are still on display.

NAA has been largely responsible for our understanding of the elemental composition of moon rocks. Samples brought back to Earth from the lunar surface by the Apollo manned space missions have been studied by NAA. The composition of lunar rocks and soil was found to be similar in composition to that of the basaltic achondrites, except that the moon materials are richer in rare earth elements and poorer in volatile elements. These samples are also still available for further studies.

The first two textbooks on NAA were written independently, one in England and the other at ORNL. The first, published in England in 1963, was *Radioactivation Analysis* by H. J. M. Bowen and D. Gibbons. The second, written entirely by ORNL personnel and edited by William S. Lyon of ORNL, was *Guide to Activation Analysis* (1964). ORNL researchers also contributed, together with scientists of other laboratories, to the preparation of several dozen *Radiochemistry Monographs* that have long been valuable to analytical chemists.

ORNL researchers over the

Larry Robinson listens as Juel Emery explains the layout for the enlarged Neutron Activation Analysis Laboratory at the HFIR.

years have studied the probabilities that elements will absorb neutrons and become activated and have developed "cross sections" that detail this information. These "cross sections" have contributed to the body of knowledge about the suitability of sample types for analysis by neutron activation. Results of basic studies of NAA carried out at ORNL have been published in U.S. and foreign journals and reported at many international meetings.

Reactor irradiation can be used to measure more than 65 elements at part-per-million levels and many in the part-per-trillion range. Although reactors are most often used for NAA, other neutron sources include machine neutron generators and isotopic sources such as californium-252 (which is produced at the HFIR). Other neutron sources, which are commonly used by industry, are less sensitive but much cheaper and easier to operate.

NAA Facilities at ORNL

At ORNL, NAA was first performed at the old Graphite Reactor (now a National Historical Monument). Since 1958, NAA at ORNL has been performed using a pneumatic tube system at the Oak Ridge Research Reactor (ORR). In 1970 a similar irradiation system was installed in the HFIR. That system, which is still in use, has the highest neutron flux (5×10^{14} neutrons/cm$^2 \cdot$ s) and, thus, the highest analytical sensitivity of all pneumatically operated systems in the world. The ORR laboratory (and eventually the reactor) will be closed down in 1987, so an additional pneumatic tube has been installed in the HFIR to provide service to compensate for the lost system. Also, the floor space of the HFIR laboratory has been nearly tripled.

In addition to high neutron flux, the irradiation systems of the HFIR have several advantages over most similar facilities of other NAA laboratories. In pneumatic systems, samples are transferred by compressed air. In the HFIR, sample containers, or rabbits, are transferred to and from high-neutron-flux locations near the reactor core. Unlike the NAA systems at ORR and other places where the air exhausts at the ends of the tube causing the rabbits to hit the ends and break (thus limiting use to rabbits made of plastic materials), the pneumatic tubes of the HFIR exhaust air 0.3 m (1 ft) or more from the ends. Air is blown in both ends of the tube causing the rabbits to stop at the exhaust port on counter-current columns of air. Air exhaust ports are located near the reactor core, for neutron irradiation; in the laboratory, for loading and retrieval of rabbits; and in the reactor pool, where rabbits are sometimes left temporarily following irradiation to allow highly active short-lived radionuclides to decay before the rabbit is returned to the laboratory.

Because they encounter gentle conditions in the pneumatic tube, rabbits can be made of graphite. Although graphite rabbits were prepared and used in the old HFIR system beginning in 1971, the graphite was not tough enough and the rabbits tended to develop cracks. Occasionally one would break and contaminate the system. About three years ago, ORNL radiochemists obtained rabbits from Poco Graphite Company that revolutionized irradiations in the HFIR. "These rabbits are very tough and pure," says Dyer. "They do not break after many long irradiations and they contain almost no elements that become radioactive."

Thus, the new graphite rabbits have provided a reliable way to make irradiations in either of the HFIR pneumatic tubes for essentially unlimited durations, allowing the analytical measurement sensitivities for elements that yield long-lived radionuclides to be pushed to nearly any level necessary. If only a few minutes of irradiation time are needed (e.g., in delayed neutron counting, which requires irradiations lasting only 30 to 60 s), polyethylene rabbits can be used. The chief advantage of using these plastic rabbits is that they are much less expensive than graphite rabbits ($0.50 per plastic rabbit vs $12 per graphite rabbit).

Because the new pneumatic tube's irradiation station is farther from the core than the old one, the neutron and gamma-ray flux is lower. As a result of the lower "gamma heating," the plastic rabbits are much less likely to melt or deteriorate during irradiation. Although plastic rabbits have always been used in the old HFIR system for small samples and short irradiation periods, the effects of gamma heating on them has been a problem. Now that this problem is solved by the new pneumatic tube, plastic rabbits will be used more

Jim Eldridge and Joe Northcutt examine a moon rock that was analyzed for radionuclides. Moon rocks were also analyzed by NAA for their elemental content.

often and for larger samples and longer times without fear that they will contaminate the system.

ORNL's Use of NAA for Semiconducting Materials

Analysis to determine the content of natural uranium and thorium in aluminum and silicon, two principal materials used to make computer memories, is an example of a measurement in which very low sensitivity is required. Four principal methods make use of neutron irradiations to determine trace concentrations of uranium. Two of these are classified as conventional NAA methods. In one, the uranium-238 (^{238}U) isotope absorbs a neutron and becomes ^{239}U, which decays to neptunium-239 (^{239}Np). The induced ^{239}Np radioactivity is measured and used to derive the uranium concentration. A similar measurement is made for thorium (Th) after ^{232}Th absorbs a neutron and becomes ^{233}Th, which decays to protactinium-233 (^{233}Pa). Gamma radiation from the ^{233}Pa is measured and used to calculate the thorium concentration.

Other methods for measuring uranium content rely on the fissioning of the ^{235}U isotope. In one method, the gamma rays from one of the isotope's fission products are measured and used to calculate the uranium concentration. Although this method is considerably less sensitive than the one based on ^{238}U and is seldom used, it is subject to far fewer interferences and is sometimes needed for certain types of samples. The two other methods for determination of uranium concentrations—delayed neutron counting and fission track analysis—are also based on the fissioning of ^{235}U.

Delayed neutron counting (DNC) was a "bread and butter" feature of the old ORR pneumatic tube that has been designed into the new HFIR facility. The method is one of the simplest of all measurements of analytical chemistry and is the most rapid and economical method for determining trace concentrations of uranium in matter. DNC is based on the fact that, when a sample containing ^{235}U is exposed to neutrons, some of the nuclei of the ^{235}U will fission, emitting additional neutrons. Most of the neutrons are emitted instantaneously, but some are delayed in their emission and can be counted after the sample is removed from the neutron flux. Although ^{233}U and ^{239}Pu behave like ^{235}U, no significant delayed neutron emission occurs from other naturally occurring elements, and the method is unique and without interference for the determination of natural uranium (which includes ^{235}U and ^{238}U). Unlike the old HFIR laboratory, DNC in the new addition is automated, allowing the processing of many samples—from irradiation to the final result—without human intervention. Although the

Bill Lyon (now an ORNL consultant) edited the first American textbook on neutron activation analysis and, in 1981, became the fifth American scientist to win the George Hevesy Medal, an international honor conferred by the **Journal of Radioanalytical Chemistry.**

technique is not quite as sensitive for natural uranium as is conventional NAA for ^{238}U, the high neutron flux of the HFIR makes it possible to determine a few parts per billion (ppb) of natural uranium.

The combination of this analytical sensitivity with the ability to make an analysis in less than five minutes (i.e., weighing, irradiating, counting neutrons, and calculating results) and the lack of interferences to the method suggests that the new irradiation system of the HFIR is a powerful analytical tool for uranium measurement. Efforts are under way to evaluate the system for measuring uranium concentrations in semiconductor memory materials.

The fourth method of using neutrons to measure trace levels of uranium is called fission track counting. This method, which is being used by ORNL researchers to

Dyer holds a plastic rabbit used for irradiations of samples in the High Flux Isotope Reactor.

determine uranium content in refractory materials, is based on the fact that fission fragments, formed when ^{235}U fissions, can escape from the surface of the sample when the fission occurs close to the surface (within about 15 μ). Most of the fragments that escape have very high energies and can damage tiny regions and leave tracks in materials, such as glass or plastic, that are placed in contact with the sample. The material that is damaged is referred to as a fission-fragment track recorder or simply track recorder. Many track recorders can be etched by chemical reagents to make the tracks visible under a microscope. The number of tracks per unit area, or the "track density," can be determined for a sample having an unknown quantity of uranium by comparing it with the track density of a standard (containing a known ^{235}U concentration); from this information the uranium concentration in an unknown sample can be computed. The sensitivity of the track density method is greater than DNC and is comparable to the conventional NAA method for ^{238}U. Natural uranium concentrations as low as 0.01 ppb are easy to determine in the HFIR irradiation systems.

A synthetic quartz called Supersil I made by Amersil, Inc., has been found to be one of the most useful track recorders. Supersil I contains no measurable uranium and is being used to determine uranium in materials consisting of compounds of tungsten, tantalum, vanadium, molybdenum, and silicon. These elements, sometimes called refractory materials because of their chemical inertness, are new candidates for use in computer memories because they can withstand extreme conditions such as high temperatures. Currently no practical alternative to fission track analysis appears available for determining ppb levels of uranium in these refractory materials.

Using NAA, ORNL has been analyzing aluminum and refractory materials manufactured by Comenco Electronics, Varian Associates' Specialty Metals Division, International Minerals and Chemicals Corporation, ALCOA, and Harbison-Walker Refractories, a division of Dresser Industries. These companies are developing processes to make semiconducting materials that can be sold to the computer industry.

"One of the main interests of semiconductor manufacturers is to eliminate use of raw materials that have high levels (more than 1 ppb) of uranium and thorium because their alpha-particle emissions create soft errors in memory devices," says Emery. "We are working with vendors of materials like aluminum. They are trying to develop processes to make high-purity materials free of uranium and thorium. We analyze the product of their process and give them feedback, so they can determine whether and where the process needs improvement."

NAA and Reactors

NAA is a product of the nuclear energy program; it thrives because of the availability of research nuclear reactors. But the reactor industry also owes a debt to NAA.

In 1947 a type of NAA experiment was carried out at ORNL to determine the ability of a material to absorb neutrons. Physicist Herb Pomerance was studying zirconium, which was considered a promising material for cladding reactor fuel because it can withstand high temperatures and resist corrosion. The question was, Does zirconium absorb a negligible amount of neutrons? If so, it would be an ideal cladding material. Using a pile oscillator as a neutron source, Pomerance found that pure zirconium absorbs only a few neutrons (low cross section) but that hafnium, which normally contaminates the zirconium extracted from ores, is a reactor "poison" because it absorbs a high number of neutrons (high cross section).

As a result of Pomerance's findings, ORNL researchers at the Y-12 Plant developed a process for separating hafnium from zirconium, thus producing a highly suitable cladding material. The Oak Ridge process is still used throughout the world, and zirconium-clad rods of uranium pellets constitute the fuel cores of virtually all light-water reactors.

Neutron activation analysis remains a useful technique today 50 years after it was first developed, even though numerous other analytical techniques have been developed in the meantime. And ORNL scientists continue to develop ways of using NAA and strive to understand both its limitations and its benefits.

ORNL's Forays into Forensic Science

Triplets!! Not one suspect, in the shooting of a storekeeper and a policeman, but three!

Dick Tracy: . . . We've got problems! Who fired that gun?

Lizz: A PARAFFIN test?

Dick Tracy: NEVER! That test is DEAD as the dodo! —Never was dependable. Today's test, known as the neutron activation analysis, is brand new and accurate.

Will it reveal the guilty triplet?—Dick Tracy, *San Francisco Sunday Examiner & Chronicle*, August 22, 1971.

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Is neutron activation analysis (NAA) a reliable tool for solving crimes, as Dick Tracy suggests? Several radiochemists have given this question considerable thought over the years. Their conclusions are based on experiences that have never before been reported extensively. In the 1960s ORNL radiochemists used neutron activation analysis to examine evidence from the assassination of President John F. Kennedy. They also rendered opinions in federal court on whether NAA evidence should be accepted in two sensational murder trials. Through these experiences, they became more aware of the limitations as well as the benefits of NAA for forensic science.

The Kennedy assassination. Like millions of people, Frank Dyer of ORNL's Analytical Chemistry Division remembers where he was when it happened. He says he was walking between Buildings 4501 and 4500 North at around 1:30 p.m. on November 22, 1963, when he heard the shocking news on the public address system: President Kennedy had been shot while riding in an open limousine in a motorcade in Dallas, Texas. Later Dyer learned that the President had died and that the accused assassin was Lee Harvey Oswald, who had been seen firing a rifle from the sixth floor of the Texas School Book Depository and later shooting a revolver on the street, killing Patrolman J. D. Tippit.

Little did Dyer know at the time that the assassination would affect the work that he and his colleague, Juel Emery, would be doing for the rest of 1963. The next week their supervisor, Bill Lyon, was called to Washington, D.C., where he was told in strictest confidence that the Federal Bureau of Investigation (FBI) laboratory in Washington needed the assistance of ORNL. FBI agents had confiscated paraffin casts of Oswald's hands and face from an employee of the Dallas Police Department. They also had collected lead fragments of the two bullets that had struck Kennedy (one of which also wounded Texas Governor John Connally) and the one that missed.

Lyon learned that this evidence, which was in Washington, was to be brought to Oak Ridge by FBI chemist Jack Gallagher. The FBI wanted ORNL radiochemists to use NAA to (1) verify that Oswald was the person who fired the rifle that killed the President and (2) determine whether the three fired bullets all came from Oswald's rifle. For five weeks Gallagher worked with ORNL radiochemists Dyer and Emery on the secret project, which included the firing of weapons. Gallagher may have broken the record for guest occupancy at the Holiday Inn in Oak Ridge.

A paraffin cast is made by applying molten paraffin to the skin, allowing it to cool and harden, and then peeling it off. If gunpowder residue is present on the skin, the residue will stick to the warm paraffin and show up on the cast as blue specks after treatment with diphenylamine or diphenylbenzidine. Either chemical will turn blue in the presence of nitrates from the

gunpowder. (It had long been thought that the blue dots indicate that the suspect recently fired a weapon; however, paraffin tests are no longer considered reliable because nitrates from sources other than weapons may also be present on the skin.)

The FBI hoped that the ORNL researchers could extract samples of gunpowder residue from the paraffin casts and analyze them using NAA at the Oak Ridge Research Reactor. Neutrons from the reactor would activate the elements in the gunpowder, causing each one to emit characteristic gamma rays that could be detected by a sodium iodide gamma spectrometer and analyzed by a multichannel analyzer. Spectra of the gamma rays

Dyer, Lamont Bate (deceased), and Emery examine paraffin casts of hands after firing weapons in late 1963. They made the casts to understand how gunpowder residue is scattered from fired pistols and rifles such as were used by Lee Harvey Oswald, President Kennedy's assassin.

reveal which elements—and how much of each—are present.

Specifically, the ORNL researchers were to look for the ratio of antimony to barium in the gunpowder primer (the primer consists of barium nitrate and antimony sulfide). It was hoped that comparison between the barium-antimony ratio of the gunpowder residue on Oswald's hands and face would match that of the gunpowder used in the 6.5-mm Mannlicher-Carcano rifle that killed Kennedy. The FBI had evidence that Oswald had purchased the rifle but still sought additional physical proof that he actually handled it at the time of the assassination. (Oswald's right palmprint was discovered on the barrel of the rifle.)

"The paraffin casts presented us with a problem of logic," said Dyer. "Everyone knew that Oswald fired a pistol as well as possibly the rifle. Witnesses saw him with the revolver that killed Patrolman Tippit. So for us, finding antimony and barium on the paraffin casts of Oswald's hands and right cheek was not a big surprise because we already knew he had fired a weapon. From the beginning, it seemed practically impossible to make a correct interpretation from the data."

According to Emery, "One problem with rifles is that they do not emit as much residue as pistols. Gunpowder residue is broadscattered from pistols but little residue from rifles gets on the hands of users."

At the Laboratory Dyer, Emery, and several FBI agents learned about these problems after firing pistols and rifles and making paraffin casts of their hands. "Ironically," says Dyer, "the largest deposit we found was on the hand of an FBI man who had not fired a gun but had simply handled it. We saw a big speck on the paraffin cast from his hand and decided to check it out. It had massive amounts of antimony and barium in it."

Interpretation of the results was also made difficult because the ORNL radiochemists found the antimony and barium not only on the cheek side of the paraffin cast but also on the side not contacted by Oswald. The residue seemed to be smeared all over the cast, indicating that the cast had been improperly prepared or handled. In fact, the FBI did not obtain the paraffin casts until after they had been tested by the diphenylamine test and taken home by a Dallas police technician who wanted to keep them as collectors' items.

"If we had received the casts before anyone else handled them," says Dyer, "it is possible that by obtaining and comparing barium-antimony ratios using activation analysis, we could distinguish between ammunition from Oswald's pistol and ammunition from his rifle and thus verify that he had shot the rifle. If the ammunition in the rifle differed from that in the pistol, we might have been able to conclude that Oswald fired both the pistol and the rifle. But since the paraffin casts had been mishandled so grossly, we didn't think we had good enough evidence to make a valid conclusion. So we chose not to make an interpretation of the evidence."

The work at ORNL was mentioned in the *Report of the President's Commission on the Assassination of President Kennedy* published in 1964 (page 562):

"The paraffin casts of Oswald's hands and right cheek were also examined by neutron-activation analyses at the Oak Ridge National Laboratory. Barium and antimony were found to be present on both surfaces of all the casts and also in residues from the rifle cartridge cases and the revolver cartridge cases. Since barium and antimony were present in both the rifle and the revolver cartridge cases, their presence on the casts was not evidence that Oswald had fired the rifle. Moreover, the presence on the inside surface of the cheek cast of a lesser amount of barium, and only a slightly greater amount of antimony, than was found on the outside surface of the cast rendered it impossible to attach significance to the presence of these elements on the inside surface. Since the outside surface had not been in contact with Oswald's cheek, the barium and antimony found there had come from a source other than Oswald."

"In a nutshell," says Lyon, "the five-week exercise showed what every chemist always knows: bad sampling plus good analysis equals wasted time."

In addition to the paraffin casts, the FBI brought to Oak Ridge the bullet fragments found in the President's limousine, including one scraped from the windshield. At the time, several people proposed the idea that Oswald might not have been alone in shooting the President, that he may have been part of a conspiracy. So, the FBI was interested in any evidence that would show whether the bullets came from a single rifle—or from more than one weapon. ORNL's job was to use NAA on all the lead fragments and compare it with residue from a cartridge case fired from Oswald's rifle by an FBI agent following its confiscation.

"The lead used to make bullets contains antimony to harden the lead and silver as an impurity," explains Dyer. "Lead-based materials from different manufacturers of bullets were thought to contain different ratios of silver to antimony. We found no indications from our NAA studies that the lead in the three fired bullets came from different sources. So we concluded that the three bullets came from the same rifle." This conclusion, which has since been corroborated by others, has stood the test of time.

Several years ago, Vince Guinn, an NAA specialist at the University of California at Irvine (who can be seen in a 1967 movie on forensic activation analysis made for the Atomic Energy Commission), evaluated the ORNL work in connection with the Kennedy assassination and reported on it at a Laboratory seminar. "All our results, the paraffin casts, and lead fragments were kept by the FBI for national security reasons, so Guinn had to go to the FBI to evaluate our work," said Dyer. "He found some small inaccuracies in our work but agreed that our results were essentially correct."

Two well-publicized murder cases. The first known use of NAA for solving crimes occurred in Canada in 1959 when an attempt was made to match the trace-element content of hairs found at the site of a murder with that of hairs from the suspect. Details of this bit of nuclear sleuthing are described in an article in the *Royal Canadian Mounted Police Gazette*. In the 1960s NAA evidence was obtained for numerous murder cases. By 1969 NAA evidence had been accepted in court 28 times. The folly, says Dyer, is that some defendants have been convicted, perhaps wrongfully, because of the misuse of the NAA evidence that was admitted.

After the Kennedy assassination, Dyer became increasingly aware of the limitations of NAA for forensic uses. He saw how easily NAA results could be misinterpreted. "Some attorneys and jurors thought the peaks and valleys of gamma-ray spectra taken with sodium iodide detectors represented a pattern similar to fingerprints. They were attracted to spectra because they could be easily compared visually.

"Actually, gamma spectra represent statistically uncertain numbers that are proportional to the amounts of a few trace elements. Also, much of the pattern results more from the properties of the electronics and detector than from the actual trace-element concentrations."

In 1965 Dyer and his ORNL colleagues were among the first to point out the difficulties in using trace-element ratios for matching something found at the scene of the crime with something associated with the suspect. "Ratios are subject to large statistical errors and are not unique. For example, a paint sample having 2 ppm of copper and 4 ppm of cobalt looks the same as another sample that has 300 ppm of copper and 600 ppm of cobalt when the ratios of copper and cobalt are compared. In other words, the trace-element concentrations themselves, not the ratios, should be compared."

Dyer and his associates also recognized that statistical methods were needed to (1) quantify the degree of similarity of a test sample and a control or source and (2) differentiate the source from other sources. For example, if it can be demonstrated after evaluating a large body of data that only 10% of the population has hair containing trace-element concentrations that cannot be distinguished from those in the hair of the suspect, then it can be shown with a high degree of probability that the hair at the scene of the crime that matches the hair of the suspect indeed came from the suspect. In the late 1960s statistical methods for dealing with NAA results were developed in England.

In June 1966 Dyer had an opportunity to use his expertise to evaluate NAA evidence being considered for use in a murder-rape trial. He served as a defense expert in Houston in the case in which Henry Amerson, a former airplane mechanic, had been accused of raping and murdering Marjorie Wills, a flight insurance clerk, at Houston International Airport on January 16, 1965. The State of Texas attempted to introduce NAA evidence to show that hairs found in Amerson's car came from the head of the victim, that hair matching that of Amerson was found on her clothes, and that a thread on her hand matched threads on one of his garments.

Dyer, who was in the courtroom when the jury was absent, sat next to the defense attorney, Richard Haynes, while the state's expert was examined and cross-examined, to allow the judge to decide if the NAA evidence could be admitted in the trial. The expert was a radiochemist at Texas A&M University who argued that the ratios of trace elements that he found in two hair samples showed that the hairs found in the car came from the victim.

Following Dyer's counsel, Haynes pointed out the problems with ratios and the lack of a large body of data. The judge decided not to admit the evidence. Says Dyer, "This was the first Texas case to consider trace-element evidence. The next year, in another Texas murder-rape case, NAA evidence was admitted and the jury found the defendant guilty. He was sentenced to die in the electric chair. Newspaper accounts that I read indicated that the NAA evidence was instrumental in his conviction."

Says Dyer: "The problem now in matching physical evidence samples like hair by their trace-element content lies not in the method used to measure the trace elements, whether it be NAA, mass spectrometry, or whatever. Nor does it lie in the statistical method of comparing the data because methods of comparison are well known. The crucial problem is the absence of a large data base of trace-element concentrations in any particular material that becomes the subject of crime investigation.

"The population of trace elements in such materials must be known to interpret the data and judge whether samples match. Because almost any material can become the subject for a comparison, almost everything would need to be analyzed; thus, the number of measurements that would be necessary is simply too large to be economically feasible. It seems likely too that the populations of trace elements in some materials might change with time, making previous measurements obsolete."

In April 1969 ORNL's Enzo Ricci, Lamont Bate (deceased), and Dyer served as defense experts at a murder

***ORNL radiochemists Emery and Dyer reminisce about their studies of the Kennedy assassination evidence, the results of which were published in the* President's Commission Report on the Assassination of President Kennedy.**

trial in Cleveland, Ohio. In this case tried in federal court, the defendant Orville E. Stifel II, then a 22-year-old former laboratory technician at Procter & Gamble Corporation in Cincinnati, was charged with sending a bomb through the mail to kill Daniel J. Ronec, the fiance of a woman with whom Stifel had formerly been romantically involved. James Scott, a chemist for the U.S. Post Office Department who had experience analyzing the trace-element content of tape, used NAA to analyze pieces of red vinyl tape, a gummed mailing label, cardboard, and metal fragments found after the bomb killed Ronec. Scott testified that the amounts of the trace elements in these materials were the same as those measured in similar tape, mailing labels, cardboard mailing tubes, and metal lids on tubes found at a Procter & Gamble plant where the defendant had worked.

The evidence had already been admitted when the ORNL radiochemists were called to testify. Ricci, Bate, and Dyer told the jury that the evidence, primarily a comparison of plots of gamma spectra, met none of the statistical criteria for valid comparisons developed two years before in England. Despite their efforts to convince the jury that the NAA evidence was nonsense, Stifel was found guilty and sentenced to life in prison. He appealed his conviction in 1970, arguing that the NAA evidence should have been ruled inadmissible. In 1984 the judge of the U.S. District Court of Northern Ohio agreed that Scott's methods lacked credibility and granted Stifel a new trial. In a November 2, 1984, letter to Ricci, Stifel wrote, "At long last, after sixteen years, the court granted my Section 2255 motion and vacated my conviction . . . None of this would have been possible without you."

Perspective on NAA for forensic science. During the 1960s the Nuclear and Radiochemistry Analysis Group at ORNL received many requests for assistance involving NAA. "These requests," said Lyon, "were primarily due to the group members' excellent publications and conservative approach to the subject. Most of these requests had to be turned down, especially those of private individuals."

Lyon recalls two bizarre incidents involving private persons. "A husband and wife from Nashville brought a cake to the ORNL group and requested that it be analyzed for poison. The cake had been sent to a relative who became sick. The second case involved parents of a man in Pennsylvania who had been declared criminally insane and had been given a lobotomy. The parents had evidence that the man had not committed any crime and wanted the evidence reexamined using NAA."

With the increase of reactors in the 1970s came more labs and experts in forensic NAA. So the ORNL group relinquished its activity in this area to those commercial ventures. The position at ORNL was best expressed by an impromptu remark by then Laboratory Director Alvin Weinberg who, when he heard at an information meeting that the AEC wanted NAA work done on hair analysis, called out from the auditorium floor, "Not us!"

For years the FBI laboratory refused to use NAA for hair and only slowly did it accept the technique for other samples. Despite Dick Tracy's optimism, NAA still remains somewhat controversial and subject to differing interpretations—*C. K.*

awards and appointments

Three ORNL inventions were named among the top 100 research and development achievements in 1986 by *Research & Development* magazine, bringing to 55 the total won by Department of Energy facilities since 1967. The ORNL award-winning developments and inventors are an integrated gas analysis and sensing chip by **Robert J. Lauf** (Metals and Ceramics Division), **Barbara S. Hoffheins** and **Michael S. Emery** (Instrumentation and Controls Division), and Melvin W. Siegel (Carnegie-Mellon University); a multimode ionization detector by **Michelle V. Buchanan** and **Marcus B. Wise** (Analytical Chemistry Division); and a soft X-ray emission spectrometer by **Tom A. Callcott** (University of Tennessee and Health and Safety Research Division), **Edward T. Arakawa** (Health and Safety Research Division), Ken L. Tsang (University of Tennessee), and David L. Ederer (National Bureau of Standards).

Walderico M. Generoso has been appointed a member of the National Research Council's Commission on Life Sciences' Panel on Reproductive and Developmental Toxicology of the Committee on Biological Markers.

Several ORNL researchers have been appointed to positions by the American Society for Heating, Refrigerating, and Air-Conditioning Engineers. They are **Van D. Baxter** (program chairman for Applied Heat Pump/Heat Recovery Systems and chairman of the Task Group on Latent Source Heat Pumps); **George E. Courville** (program chairman for Measurement and Instruments and for Thermal Insulation and Moisture Retarders); **Fred Creswick** (chairman for Unitary Heat Pumps and Air Conditioning); **H. Perez-Blanco** (chairman for Absorption and Heat-Operated Machines), and **E. A. Vineyard** (chairman of the symposium on Strategies for Reducing Energy Costs for Large Building Air-Conditioning Systems and program chairman for Large Building Air-Conditioning Systems and for Domestic Refrigerators and Food Freezers).

Steiner J. Dale has been appointed chairman of the Gaseous Dielectrics Committee of the Institute of Electrical and Electronics Engineers, Inc. (IEEE), chairman of the IEEE Insulated Conductors Committee, and general chairman of the 1986 International Symposium on Electrical Insulation.

G. Daniel Robbins has been elected director of the Chapter Assembly of the American Society for Information Science (ASIS). The Chapter Assembly is the coordinating body for all ASIS chapter activities.

Charles R. Weisbin has been named director of ORNL's new Robotics and Intelligent Systems Program.

Enzo Ricci has been appointed member of the Executive Committee of the American Nuclear Society (ANS) and of the Executive Committee of the ANS Isotope and Radiation Division.

Hal Haselton, **Chris Foster**, and **Stan Milora** have received Distinguished Associate Awards from the Department of Energy for their "outstanding contributions" to the nation's magnetic fusion energy program. Haselton was recognized for "development, design, fabrication, installation, and operation of plasma heating and fueling equipment," and Foster and Milora were cited for "design, development, fabrication, installation, and experimental demonstration of hydrogen pellet injectors."

Lee Berry has been named a member of the 1986 Executive Committee of the American Physical Society.

The group responsible for the design and construction of the Advanced Toroidal Facility (ATF) in ORNL's Fusion Energy Division has received an Energy Resources Technology Award from the American Society of Mechanical Engineers. The ATF group was recognized for "contributing one of the most outstanding examples of advancing mechanical engineering."

George E. Courville has been appointed chairman of DOE's Thermal Mass Review Panel.

Marilyn Brown has been appointed to the editorial board of the *Annals of the Association of American Geographers.*

Jerry Elwood, William Fulkerson, Carl Gehrs, Elias Greenbaum, Elizabeth Peelle, and **Tom Wilbanks** have been named Fellows of the American Association for the Advancement of Science.

N. B. Gove is chair-elect of the Special Interest Group on Numerical Data Bases for the American Society of Information Sciences.

Eric Hirst has been named associate editor of *Energy* and appointed to the editorial boards of *The Energy Journal, Energy Policy, Energy Systems and Policy, Evaluation and Program Planning,* and *Journal of Environmental Systems.*

D. W. Jones has been appointed to the editorial advisory board of *Indian Journal of Landscape Systems.*

Bob Langley is president-elect of the American Vacuum Society.

Steve Rayner has been appointed corresponding editor for the *Research Papers Series.*

John Sorensen has been named University Fellow of Colorado State University.

Tom Wilbanks has been asked to chair the Task Force on Geographic Advice on National Issues and the Honors Committee of the American Association of American Geographers. He has also been appointed advisory editor of the *Syracuse Geographical Series.*

In ORNL's Fuel Recycle Division, **William S. Groenier** has been named head of the Chemical Process Development Section and **Sam A. Meacham** has been named head of the Remote Systems Development Section.

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In 1958 Sen. John F. Kennedy and his wife Jacqueline Bouvier Kennedy visited ORNL and toured the Oak Ridge Research Reactor. Here, Kennedy chats with then ORNL Director Alvin Weinberg while Sen. Albert Gore, Sr., talks to Mrs. Kennedy. Looking on at left is Sam Hurt, who today is the Operations Division experiment coordinator. In late 1963 the FBI asked ORNL scientists to help in the investigation of the assassination of President Kennedy. See article on page 48.