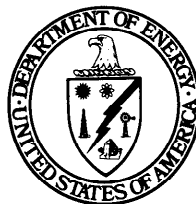


# Health & Environmental Research

## Summary of Accomplishments

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The purpose of this brief narrative is to foster an awareness of a publicly funded health and environmental research program chartered nearly forty years ago, of its contributions toward the national goal of safe and environmentally acceptable energy development, and of applications of its findings toward the improvement of human health. This program, administered by the Office of Health and Environmental Research, in short, OHER, is one of many research activities of the U. S. Department of Energy (DOE). Over the years this program has been sponsored by other federal agencies responsible for the national energy mission. Its evolution has been a reflection of changes in time, in public priorities, and in Congressional mandate. But, throughout this evolution, there has remained a consistency of purpose: to seek a fundamental understanding of the health and environmental aspects of emerging energy technologies and to establish the body of knowledge necessary to the development and utilization of the technology consistent with the public health and safety.

The story of this research program can be told through its accomplishments. Several of the more significant of these accomplishments have been chosen here for illustrative purposes, including some whose value has far exceeded the cost of the research program itself. However, regardless of the measure of its economic benefit, the basic motivation for the program remains to *serve the public interest* through health and environmental research. In the few pages that follow, the selected accomplishments are grouped and reviewed within each of several areas of research.

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## Executive Summary

This is a short account of a 40-year-old health and environmental research program performed in national laboratories, universities, and research institutes. Under the sponsorship of the federal agencies that were consecutively responsible for the national energy mission, this research program has contributed to the understanding of the human health and environmental effects of emerging energy technologies. In so doing, it has also evolved several nuclear techniques for the diagnosis and treatment of human ills.

The form of this presentation is, literally, through "snapshots"—examples of significant, tangible accomplishments in each of these areas at certain times to illustrate the role and impact of the research program. The program's worth is not necessarily confined to such accomplishments; it extends, rather, to its ability to identify and help solve potential health and environmental problems before they become critical. This anticipatory mission has been pursued with an approach that combines a commitment to fundamental research that is long term and high risk with applied problem solving.

The narrative of this research program concludes with a perspective of its past and a prospectus on its future.



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## Origins of the Research Program

The origins of the Office of Health and Environmental Research trace back to the outset of the Second World War and the establishment of nuclear research centers under the "Manhattan Project." The first formal program began in 1942 as a Health Division, established by Dr. Arthur Holly Compton, Director of the University of Chicago Metallurgical Laboratory. Already a Nobel Laureate for his work on X-ray scattering, Dr. Compton recognized the unprecedented hazards posed by radiation to wartime workers at the laboratory. With the perspective of a half century of earlier experience with X rays and radium, he and his colleagues could well appreciate the dangers as well as the possibilities of atomic radiation. Biomedical programs were soon established at Oak Ridge, Tenn., and in the Manhattan Project at large, and it is fortunate that these programs were able to attract the most competent physicians and medical researchers in the field of the biomedical effects of radiation.

Like the Curies and other pioneers in the field of radiation, those who sought to protect the health of their colleagues could understand, more than others, that the phenomenon that so concerned them was, at the same time, an opportunity. They grasped its significance and foresaw the promise of radiation and nuclear medicine as a new means for medical diagnosis and treatment. This promise has been fulfilled. Today nuclear medicines are produced and packaged in myriad forms and are in widespread use; for example, thallium-201 alone was administered to 370,000 patients in 1981 for the diagnosis of heart disease.

In providing the first legislative basis for the health research program through the Atomic Energy Act of 1946, the Congress overlooked neither the opportunities nor the dangers presented by radiation. In the act the Congress directed the Atomic Energy Commission (AEC) to

*. . . make contracts, agreements, arrangements, grants-in-aid, and loans . . . for the utilization of fissionable and radioactive materials for medical and health purposes . . .*

and for

*. . . the protection of health during research and production activities . . . .*

The need for a highly qualified group of research administrators was foreseen to fulfill this broad charter. Thus the Division of Biology and Medicine was established, and Dr. Shields Warren, Professor of Pathology at Harvard, was named its first director. Under Dr. Warren the division laid down the outlines of a vigorous research effort in fundamental studies in the life sciences, in applied areas to ensure industrial hygiene in AEC facilities as well as the public health and safety, and in fostering the rapid growth of nuclear medicine.

The responsibility for administering this program was later assigned to the Energy Research and Development Administration (ERDA), which succeeded the Atomic Energy Commission through the Energy Reorganization Act of 1974. The oil embargo, however, had underscored the need for developing a wide range of energy options and technologies in addition to nuclear, and this was reflected in the new agency's mission. Therefore this act charged the ERDA administrator with the additional responsibility of

*. . . engaging in and supporting environmental, physical, and safety research related to the development of energy sources and utilization technologies.*



These responsibilities were assumed by the agency's Division of Biomedical and Environmental Research, which initiated a significant program of nonnuclear research, focusing on the development of fossil fuels and renewable energy sources. At the same time, a broad range of legislation\* strengthened and expanded the rationale for ERDA's program of health and environmental research by establishing a regulatory framework by which the results of this research could be integrated directly into the planning and development of energy technologies.

Although the Energy Research and Development Administration was relatively short lived, these research functions were retained intact by the new Department of Energy, which was established in 1977. Within the Department of Energy, these responsibilities have been carried on by the Office of Health and Environmental Research.

What, then, has been the net result of OHER's history of changing roles and mandates? A central mission has evolved, requiring the integration of three fundamental areas of study: (1) the *source*, or the potentially toxic agent of concern; (2) its *transport*, or the path from its point of release; and (3) the *effects* that it could produce upon populations and on the environment.

The first of these areas involves the understanding and characterization of the material, pollutant, or agent of concern. Despite the seemingly limited scope of this phase of study, unexpected rewards of a much broader nature can result from this research. For example, the OHER mandate under the Atomic Energy Act required an understanding of radiations of various kinds and of

\*This legislation, beginning with the National Environmental Policy Act in 1969, included the Clean Air Act, Safe Drinking Water Act, Toxic Substances Control Act, and the Resource Conservation and Recovery Act.

their interactions. This in turn created a need for the development of a host of radiation detection instruments, some of which became essential to the field of nuclear medicine, as noted later.

The second facet of the mission, source transport, began as an effort to understand the paths that might be taken by radioactive materials through the environment. As the range of energy options under development increased, however, the transport of materials from other technologies, such as coal fly ash, combustion gases, and synthetic fuel components, also came under study.

The final segment of OHER's integrated mission is to determine the nature and the extent of the potentially toxic source materials on man and his environment. Once again, initial research in this area was confined to radiation biology—the study of mechanisms and magnitudes of effects produced by radiation. These studies included the uptake and distribution of radioactive materials in animals and in man to determine potential toxicity. This knowledge, when coupled with developments in nuclear instrumentation, provided the basis for the development of nuclear medicine, which was but one of the new directions in research to receive its impetus from radiation biology. The quest for answers to the mysterious response of cellular DNA to radiation spawned an unparalleled research program in basic genetics.

Thus the objective of the OHER mission has been straightforward—to perform fundamental research on the energy-related triad of *source-transport-effect* and to integrate its basic findings toward the solution of practical questions. The descriptions of program accomplishments that follow provide a glimpse of some of the more tangible products of this research process. But, with the background for the presentation of these products provided, some caveats are first in order.

As in any other research enterprise, there is a continuum of effort, and a "snapshot" of selected OHER program accomplishments can easily create a distorted view of the overall workings of the program. It has already been noted that, although many of the accomplishments described have proved to be of considerable economic importance, this occurrence is not necessarily a measure of the effectiveness of the research within the context of the OHER mission; nor is it a factor in shaping the OHER research agenda. The course of research is complex and can lead to a number of dead ends as well as to successes and breakthroughs. A seemingly fruitless effort can sometimes be useful, however, by virtue of its indication of more productive pathways, and one of the accomplishments described, which eventually ended in a treatment for Parkinson's disease, provides a case in point. Basic research, a key part of the program, is of a long-term nature and often contributes no immediately measurable benefit. Yet, even in the event of negative results, it adds incrementally to our storehouse of information, which, in itself, is a major accomplishment. The bone-marrow-transplantation work undertaken early in the program is an example of basic research which ultimately provided much of the information that underpins the current state of the art for organ-transplantation work in medicine.

Thus, in summarizing the accomplishments of a research program designed for a mission as far-reaching as that of OHER, one must take care to avoid judging its worth solely on the basis of economic benefit or immediate applicability. The result of research may be a tangible product (e.g., a nuclear scanner or a radiopharmaceutical) of readily calculable value. But the "product" may also be the answer to the riddle of self-repair to cell injury, the mechanism by which a particle is transported, or the definition of the risk of bone cancer from radiostrontium.

Thus it is equally valid to judge the benefit of a research contribution in terms of its reduction of uncertainty or its description of a previously unknown mechanism. These criteria have been in consonance with the energy development missions of OHER's parent agencies (AEC, ERDA, and DOE), which have made use of OHER research in an anticipatory manner to prevent, modify, or mitigate potential health and environmental effects before an emerging technology reaches maturity. The contrast between the anticipatory nature of the OHER research program and the research conducted by the regulatory agencies is readily apparent from the differing content and objectives of the respective research programs. The ultimate goal of the research program, therefore, is not so much to *find* effects as it is to aid in their *prevention*. The extent to which this goal is realized is the true measure of the program's benefit to the nation.

The following sections describe selected, definitive research contributions resulting from the OHER research program—accomplishments of the many individuals in national laboratories, universities, and research institutes who conduct this work under contract to OHER. In some instances the research has been cofunded or is now pursued under auspices other than OHER. Unfortunately, in a summary document of this size, it is not possible to give complete documentation or credit due to researcher, laboratory, and sponsor. A supplemental document of considerable length will be issued shortly which will provide such information as well as greater detail of the accomplishments themselves.

## Emerging Energy Technologies

OBJECTIVE: Through Research, Examine the Potential for Adverse Effects on Human Health and the Environment from Emerging Energy Technologies.

*It is the purpose of this Act . . . to advance the goals of restoring, protecting, and enhancing environmental quality and assuring public health and safety . . . .*

—Sec. 102, Public Law 95-91

*The functions which the Secretary shall assign . . . shall include . . . conducting a comprehensive program of research and development on the environmental effects of energy technologies and programs.*

—Sec. 203, Public Law 95-91

Thus the Department of Energy Organization Act continued the charter of a predecessor agency, the Energy Research and Development Administration. Aside from including all energy technologies, the new act identified, for the Department of Energy, responsibilities for the public health and safety which were virtually identical to those of the Atomic Energy Commission in its nuclear development and production programs. In all three charters the intent of Congress was clear: to foster a better understanding of the potentially adverse effects on human health and the environment of emerging energy technologies. The dramatic dislocations following the oil embargo of 1973 gave impetus to the development of the emerging technologies—synthetic and renewable fuels as well as nuclear—and thus added to the urgency of these responsibilities.

### Identification and Evaluation of Human Health Effects

**Nuclear Technology** The formal inception of the health and environmental research program under the Atomic Energy Commission also provided its primary focus: the study of the health effects of radiation exposure. There was more than sufficient reason.

At the outset of the Second World War, it was apparent that radiation could have adverse effects on human health. It was known that living cells could be damaged by radiation, and this phenomenon was already under study in many universities and hospitals throughout the world. The two atomic bombs detonated in wartime provided ample and tragic proof of radiation damage. The study of long-term effects of radiation on the survivors provided a wide range of dose-effect information of direct benefit to the emerging peaceful uses of the atom, including nuclear medicine and power applications. But, as we will see, in a much larger sense the study also marked the beginnings of research of the most fundamental kind, that which today holds great promise of a better understanding of biological processes and of treatments and therapies for a number of human diseases. The survivor study became an integral part of a broadly based program of research on radiation and its effects, ranging from observing the health of workers in nuclear and related industries over their lifetimes to conducting basic research to understand the fundamental processes that occur when human cells are damaged by radiation.

This research program has provided the information essential to the public debate on nuclear power. It has also provided the basis for setting radiation protection standards which have undergone constant review since their initial formulation 33 years ago. Continuing studies have reaffirmed an awareness that exposure to all radiation should be kept low; over one million people, such as nuclear shipyard workers, are currently under observation to reduce uncertainties regarding low-level radiation effects. In addition to fulfilling its primary objective of providing the information necessary to protect the health of the public and of workers in radiation environments, the body of knowledge generated on radiation effects also finds practical use in court deliberations by providing a

scientific basis upon which claims of injury can be assessed and equitable decisions can be reached.

The radiation standards themselves, though sufficiently restrictive to protect the public health, have not imposed undue economic penalty on the technology on which it has the greatest impact—nuclear electric power. More-stringent standards, which might have been necessary in the absence of knowledge gained through the research program, could have easily cost electric power consumers an additional \$2 billion annually.

It was stated earlier that research can lead to unexpected rewards. For example, research on Parkinson's disease, which originated in nuclear medicine, resulted in the discovery of a treatment that is entirely nonnuclear in nature. But perhaps no more dramatic example of unexpected benefit exists than the insights that have been gained into biological processes as the result of studies of the effects of low radiation doses. Areas that have benefited from the basic work in radiation biology include genetics and human evolution, immunology, causes of and treatment for cancer, and research on aging.

How did these seemingly unrelated benefits come together? It was already known by the early 1960's that healthy cells have ways to repair damage from certain radiations (e.g., ultraviolet). The repair, first demonstrated on exposed bacteria, was soon shown to apply to human cells. By the late 1960's, it was discovered that victims of a rare skin cancer lacked the ability to repair damage to their DNA, the substance that carries genetic information in cells. As scientists observed the effects of DNA damage, not only from a variety of radiations but also from chemical agents, it became more evident that the cell must possess a mechanism for repairing DNA. Subsequent study of the damage and repair mechanisms, and of the structure and alterations of DNA,

led to a host of theories on the possible causes of genetic diseases, birth defects, aging, and cancer, as well as advances in immunology and treatment. Much of this research may eventually resolve the question of the existence of a threshold and the ultimate expression of radiation damage.

**Synthetic Fuels** The enhanced availability and production of domestic fuels, including synthetic fuels, have remained high in national priorities for many years. The health and environmental aspects of these new energy sources, however, have required investigation because synthetic gaseous and liquid fuels have compositions that can be quite different from those of their naturally occurring counterparts. Some organic compounds in these fuels have been linked to cancer, particularly those fuels consisting of single or multiple ring-shaped molecules (cyclic and polycyclic compounds) and including other elements in addition to hydrogen and carbon. This information is needed by those concerned with industrial hygiene and public health as well as those in process development and planning. On the industrial level, early recognition of the nature of potential risks can indicate the necessity for process modifications and controls to avoid premature commitment to fixed design and thus avoid the imposition of cost-ineffective regulatory strategies.

The analysis of uncertainties in the knowledge of health and environmental risks also assists in identifying gaps and in ordering research priorities within the Department of Energy.

Several of the methods used to detect and to characterize the toxicities of synthetic-fuel components were developed within the research program of the Office of Health and Environmental Research and are described later. Briefly, a sequential strategy is employed which uses these tests in determining the toxicities of the large numbers of fuel-component samples to be evaluated.

Generally the samples are first screened through a series of easily performed cellular bioassay tests to determine whether the compounds will alter or produce toxic effects in living cells. In practical terms, this involves the physical and chemical separation of the sample into component fractions, followed (typically) by a simple laboratory test of their toxicities. On the basis of these tests, chemical fractions that demonstrate high toxicity or biologic activity and potential for human exposure are tested to determine short-term and long-term toxicities in living animals by skin painting, inhalation, or ingestion. The more elaborate studies using laboratory animals are usually undertaken when the rapid, less costly screening tests indicate that there may be a potentially important human health problem. This, briefly, is the multitiered experimental approach in wide use today.

The ultimate objective of this research is to provide sufficient information for estimating the probability of producing a specified number of health effects in a population for a given exposure to the toxic agent. This draws heavily upon risk-analysis techniques, for it involves extrapolation of animal data to estimate implications of risk for humans. If the uncertainties in this process are large, further research is required.

What, then, have been the major accomplishments in this part of the research program? We now know that some of the compounds that could be encountered in synthetic-fuels manufacture are toxic and mutagenic and that they belong to specific groups of chemicals which now have been identified. This has led to a successful search in both industry and government for methods to alter or reduce the concentrations of these compounds wherever they may occur in synfuel processes. The research program has also focused attention on the need to develop additional data on the effects of the specific synfuels pollutants identified to be of primary

concern and on the pathways and mechanisms by which the pollutants might produce such effects.

Thus the benefits deriving from the health research will be realized in terms of reducing uncertainties regarding the nature and magnitude of adverse health effects among the public and the synfuels-industry work force. The value of this reduced uncertainty, though difficult to quantify in economic terms, can nevertheless be appreciated when one merely considers the consequences of occupational exposures to cancer-causing organic chemicals in industries that were in operation before risks were clearly understood and before hazards could be adequately mitigated. For example, workers exposed to airborne emissions in coke-oven plants have shown a greater potential to develop lung cancer than the general population.

Risk analysis is developing as one possible approach to the systematic use of information to estimate potential health and environmental consequences of man's activities. Thus risk analysis, also, has become an integral part of the program of the Office of Health and Environmental Research, and this activity has also made its contribution to knowledge of synfuels effects. As an example, it has long been recognized that a portion of the particles in the air we breathe comes from coal combustion, the use of petroleum fuels in diesel and gasoline engines, and, potentially, from synfuels processing. The risk-analysis activity made use of data on the characteristics of these particles and their dispersion and transport in air to estimate the health consequences of their uptake and retention in people. Such estimates have proved particularly useful where particles pose the principal concern, as in the exhausts of automotive diesels. A related activity studied the possible consequences of substituting coal for oil as utility fuel, and here other pollutants such as sulfates (which themselves can be particles)

become dominant concerns. Eventually, what began as more limited contributions (i.e., developing methods for estimating the health effects of particles and sulfates) found application in a wide range of analyses of the risks of other pollutants, including many encountered in synfuels.

#### **Responding to Hazardous Events**

Events in recent years, such as the reentry and distribution of nuclear space debris within the Earth's atmosphere and the atmospheric testing of nuclear weapons by some foreign powers, have given rise to questions regarding our ability to evaluate and to react to such possible emergencies and their consequences. Two complementary systems that provide such a capability were developed under the OHER research program and are operational today. One, the Atmospheric Release Advisory Capability (ARAC), can predict the travel and dispersion of hazardous substances released into the atmosphere, is easily activated, and can provide results to users via direct communications. Initiated in the 1960's because of concern about fallout from atmospheric nuclear-weapons testing, the system has been expanded to provide 24-hour coverage for federal and state emergency-response support in a range of such possible situations as nuclear-weapons tests and accidents, spills of hazardous chemicals, and nuclear-power-plant releases.

The second system is designed specifically for forecasting fallout from nuclear-weapons tests and to alert federal agencies having responsibilities for monitoring, for contaminant collection and analysis, and for informing the public. Forecasting the consequences of the test is accomplished by providing relevant input to ARAC (described previously).

#### **Detection and Measurement of Human Health Effects**

Program responsibilities have required support for developing instruments and techniques to detect energy-related human health effects. These developments have found specialized use in hospitals and clinical laboratories, in research laboratories, and in government and industrial applications.

**Cell Sorting** Two instruments of this kind in use today in hospitals and clinics are the *flow cytometer* and the *centrifugal fast analyzer*. The flow cytometer was developed in 1965 to distinguish cells damaged by radiation from normal cells. Since then, the methods used for cell sorting and their applications have continued to increase. Today the flow cytometer is used routinely for complete blood counts (its greatest single application), for detecting cancer and monitoring its treatment, and for detecting genetic abnormalities. The centrifugal fast analyzer also had its beginnings in the search for tools to measure radiation effects in humans. The analyzer, which exploits advances made in centrifuge technology in the 1960's, can handle simultaneously a large number of blood samples for automated analysis. It is used principally to run blood-chemistry tests for diagnostic purposes and accounts for about 10 percent of all such tests conducted in hospitals and commercial laboratories in the United States each year. About 10,000 units are in worldwide use.

**A Fast Test for Cancer-Causing Chemicals** *Short-term cell bioassays* were developed largely for research purposes. These tests are intended as quicker and cheaper screens prior to more costly animal tests in screening for cancer-producing or cell-altering characteristics. A number of tests are included within the meaning of short-term cell bioassays. One of the most widely used of these is the Ames Test developed in this program. In this test, chemicals

are checked to see if they provide mutations in a specific line of bacteria. If they do, additional bioassay tests with cultured human or animal cells may then be employed. Short-term cell bioassays require only a fraction of the cost (an estimated \$35 million is spent annually) and time of comparable screening by animal studies, and therefore many more compounds can be screened than was possible earlier.

#### **Analyzing Complex Mixtures for Toxic Agents**

Industries and government have responsibilities requiring a range of instruments and techniques to protect human health. Two instruments, in particular, have been useful as scanners and detectors of elements in complex mixtures found in the workplace and in the environment. One of these developments is based upon an instrument in use since the 1930's, the crystal X-ray spectrometer, which identified elements in an irradiated sample by the characteristics of the reflected X radiation. In today's instrument, the crystal has been replaced by a semiconductor detector that can distinguish among many elements by producing currents which are unique to each irradiated element and which can be processed and identified automatically. Approximately 8300 semiconductor X-ray spectrometers are now in use. The average annual savings to users of these spectrometers, in terms of reduced analytical costs as compared with other techniques of elemental analysis, is estimated to be at least \$43 million. This figure is conservative since it is based on savings to only 1300 commercial users, who are in a better position than other users to estimate tangible benefits.

The other highly significant development in instrumentation, also a spectrometer, was designed specifically to identify radioactive materials. The scintillation spectrometer, commonly used for this purpose until 1965, could not distinguish well enough between radioactive elements with emissions of similar energies. Once

again, the development of new crystal detectors led to a more capable instrument, now called the *high-resolution gamma-ray spectrometer*. Today it is used widely in nuclear power plants and laboratories and by state and local agencies to monitor the environment as well as in many research applications. Based on the value of rapid analysis as compared with slower alternatives, the benefit to nuclear plant operation alone is estimated to be \$20 million annually.

**Industrial Hygiene Monitoring** The research program has also supported the development of instruments to detect and monitor toxic chemical substances. Specifically, it has supported the compilation of information relevant to instrumentation for all environmental monitoring applications. This survey has been in use as a standard for several years and will soon be issued by a private publisher. In addition, the program has supported the development of monitoring instruments specific to three important toxic chemicals which were formerly unavailable.

**Predicting Pollution Pathways in the Atmosphere** Finally, the means by which pollutants are carried and dispersed in the atmosphere have been traditionally the subject of intense study in the research program. Understanding and predicting pollutant transport are important because transport is a principal means by which health effects might be produced in the public by an emerging technology. The research program pioneered the mathematical modeling, or prediction, of pollutant behavior in the atmosphere because of the early responsibility for understanding the possible effects of radioactive contamination. But the validity of models and predictions must be tested, and in this area also the program has supported the development of the necessary tools for verification. One of these developments has been the use of nonradioactive, nontoxic, inexpensive

tracers (related to the refrigerant used in home air conditioning). These tracers are injected into the air at designated locations at known release rates, and their concentrations are later measured at other locations to determine the dispersive effects of meteorological factors, terrain, conditions of release, etc. Although gas tracers have provided valuable information of this kind, it is also known that pollutant gases often interact with minute particle clouds (aerosols) from which they may be deposited on the ground or become resuspended in air. Pollutants themselves may even originate as aerosols. Thus the program has also supported instruments to monitor aerosol behavior. The major benefit of this research has been a sounder understanding of the relationships between pollutant releases and pollutant concentrations in the human environment, information that is essential to regulation of pollutants in the general interest and for sound industrial planning.

#### **Identification and Evaluation of Environmental Effects**

Effects of emerging technologies on the environment, as well as on human health, are a prime concern of the research program. Among the major environmental issues today are the responsible uses of land and water resources. Pertinent to land use, fundamental research in soil science and plant ecology is aimed at developing an understanding of the processes that lead to changes in soils and plants.

**Riverine Ecology** In the area of water resources, fundamental research has been of value to regulatory bodies in determining to what extent rivers and other inland waters can be used for industrial cooling. In one instance, the issue was whether the impact of several operating power plants on the Hudson River would seriously damage important East Coast fish populations that inhabit the lower part of the river. The research program on riverine ecology

provided sufficient information for a reasonable estimate of this impact. These results provided a scientific basis for compromise between the Environmental Protection Agency, interveners in the proceedings, and the utilities involved.

### **Ecology of the Continental Shelf**

The continental shelf is critical to humans. Its fertile coastal waters, which account for less than 10 percent of the total ocean area, produce 40 percent of our seafood. The research, performed by a number of laboratories and universities working in specific sectors of the shelf, is well coordinated with work conducted under the auspices of other federal agencies with related responsibilities. Some fundamental mechanisms by which pollutants, as well as nutrients, enter the food chain are being established. The research program has also included studies of mechanisms by which pollutants are carried across the continental shelf into the deep ocean and of their effects on living systems. Potential benefits include a better understanding of the effects of sea disposal of municipal and other wastes, possible effects of such offshore operations as oil development, and the consequences of oil spills and of other accidental releases of chemicals in coastal areas.

### **Tracing Pathways of Nuclear Wastes in the Life Cycle**

Environmental studies in areas other than land and water use have also yielded information on the cycling of pollutants from human activities through the environment and back to humans or to other biological organisms. Several defense-related facilities process radioactive materials in the *transuranic* category (elements heavier than uranium), which are potentially hazardous to humans. Thus laboratories at the Savannah River Plant in South Carolina have for many years studied the possible uptake of these materials in the environment and the consequent potential for human ingestion. Thus far, measurements of minute con-

centrations of transuranics in the air and in crops grown in soils near these defense facilities indicate that the dose to humans is minuscule compared with that which results from naturally radioactive materials. These results have been compiled and form the basis for other determinations that may be made in the future regarding civilian and military applications of nuclear technology involving transuranic elements.

A similar situation arose with the question of the fate of other radioactive materials released in fallout from nuclear-weapons tests. Tracer research, undertaken early in the period when such atmospheric tests were conducted, led to the understanding that some elements, when transmitted up a food chain, concentrate at various levels. They can pass from one level to the next only through feeding (e.g., uptake of iodine-131 in forage eaten by dairy cows, whose milk would then be consumed by humans). This research has proved extremely valuable to the development of a better understanding of the functions of biological systems, as well as to assessments of the environmental impacts of proposed nuclear facilities.

**Plant Metabolism** A particularly useful application of radioisotope tracers has permitted a complete mapping of the pathways of carbon in the photosynthesis process. With carbon-14 as the tracer, the process from the initial fixation of carbon dioxide from the atmosphere has been followed through to the production of glucose by green plants. This understanding of the detailed biochemistry of photosynthesis laid the groundwork for new areas of investigation, such as the acceleration of plant growth and other forms of metabolic control. Another benefit provided by carbon-14 as a tracer is detailed information on intermediate chemical products and enzymes associated with both plant and animal metabolism. A spectrum of genetic engineering techniques and

developments is therefore now possible.

**Land Reclamation** Field research studies were undertaken at mining sites in three different environments: (1) a strip mine in a grassland area of Wyoming; (2) an arid area of New Mexico; and (3) in fertile Illinois farmland. The strip-mine studies have demonstrated less expensive and more effective use of topsoil in land reclamation. The potential savings through adoption of the technique in western mine areas alone could be \$600 million over the next 20 years. The studies in New Mexico showed that several kinds of hybrid plants that are highly drought tolerant could be well adapted to the reclamation of arid areas. The research in Illinois focused on techniques for returning mined, prime farmland to production. In Illinois, as in Wyoming, less expensive methods of land reclamation were found to be at least as effective as those now in practice.

### **Detection and Measurement of Environmental Effects**

#### **Detecting Change Over the Ages**

Evaluation of the effects of pollutants on the environment, as on human health, requires the development of specialized measuring techniques. Just as a radioisotope can tell of a patient's condition and tracers can give clues to the paths taken by pollutants in the atmosphere, so, too, can a similar technique give insight into geological events of long standing. Previously unanswerable questions can now be addressed. For example: How fast is land eroding? How fast are glaciers building? How old is groundwater? How fast is it replenished?

The technique that makes it possible to answer these questions uses *isotope ratios* and evolved from basic research begun in the 1950's to an understanding of long-term changes in environmental processes. Isotopes are nothing more than differing nuclear forms of the same element and therefore have the same chemical behavior, but they can be

observed individually because of their unique nuclear properties. As noted earlier, the role of carbon dioxide in photosynthesis (a chemical process) can be observed by injecting a known quantity of carbon-14 as carbon dioxide and tracing its path. This is made possible by measuring the radioactivity of carbon-14, which takes part in the process in the same way as its natural stable sister isotope, carbon-12. The measurement of radioactivity is also a measure of the quantity of carbon-14 present at any stage of the process; but the *ratio* of carbon-12 to carbon-14 tells us the *total* amount of carbon involved.

After its use in radiocarbon tracing in the early 1950's, the technique of isotope ratios found many applications in environmental geology. In quick succession it yielded histories of lake and marine sediments, knowledge of the movements of the atmosphere and underground waters, information on biological processes—in short, vital information on the paths taken by pollutants throughout the environment, the rates at which they are purged, and the extent to which they can accumulate to pose risks.



## Nuclear Medicine

**OBJECTIVE:** Develop to Its Highest Potential the Application of Nuclear Science to the Diagnosis and Treatment of Human Disease.

The phenomenon of radiation was considered by early investigators to be an opportunity for improved health care as well as a health risk. What was the basis for their optimism? Simply that a unique tool could be made available in forms convenient for use by the medical profession for diagnosis as well as the treatment of human diseases. Through nuclear medicine, it would be possible to monitor body function, to isolate the causes and extent of disease, and to subject these to a range of treatments never before possible.

### Techniques That Aid in Diagnosis

**Heart Disease** There are two major techniques for diagnosing whether patients with symptoms of coronary artery disease in fact have such disease. One involves the injection of opaque dye into an artery near the heart, after which the motion of the dye is followed by fluoroscopy. This technique, called cardiac catheterization, is painful and expensive and carries risks. The other technique, developed in the nuclear medicine program, involves injection of the radioisotope thallium-201 into the bloodstream and subsequent detection of the uptake of this tracer in cellular tissue. Reduced uptake of thallium-201 in a region indicates either reduced blood flow or damage to cells, or both. Thus the technique can detect damage to the cells of the heart and reduced blood flow to the heart. The technique is relatively inexpensive, less invasive, and low risk. Although it does not exclude the use of cardiac catheterization (which is usually required prior to surgery, once the presence of disease is confirmed), the thallium-201 scan is in wide use as a screening test, often obviating the need for catheterization. For the 370,000 patients who undergo the scan annually and avoid the necessity for more expensive catheterization, this has meant a savings of \$78 million per year in medical expenses.

**Diagnostic Scanning** The need for a versatile scanning technique, adaptive to a range of diagnostic applications, was fulfilled through the use of the radioisotope technetium-99m for imaging with the scintillation camera. The "daughter" from the quick decay of this radioisotope was found to produce low-energy electrons just sufficient for satisfactory tissue penetration and detection by the camera. With this approach it is possible to determine the amount and rate of blood flow to an area, whether an organ has normal or impaired functions, and the presence or absence of tumors, particularly in the brain, liver, and bone. At least 6 million technetium-99m studies are performed annually, representing approximately 80 percent of all nuclear medicine imaging procedures. Industry is currently producing technetium-99m with a sales volume totaling \$26 million per year.

**Hodgkin's Disease** The radioisotope gallium-67 has been used in a number of applications in nuclear medicine because it concentrates in tumors and abscesses and because of the efficient detectability of its gamma-ray emissions. Gallium-67 scanning is particularly useful in the diagnosis of Hodgkin's disease in a procedure that also permits discrimination between the various stages of this disease. The ability to discriminate is valuable because treatment is specific for each stage of the disease. The benefit of the scan to patients who have not yet reached the most severe stage of the disease, in terms of avoiding unnecessary medical expenses and losing productive time alone, is estimated to be \$10 million annually. In all applications, more than 250,000 gallium-67 scans are performed annually at a cost of \$5 million for the radiopharmaceutical alone.

### Instruments That Aid in Diagnosis

**The Scintillation Camera** The scintillation camera, named the "Anger Camera" for its inventor, was de-

vised to obtain successive images of the distribution of a radioactive tracer within the body after intravenous injection of the tracer. Thus it is used widely in conjunction with the diagnostic tracer techniques described earlier (thallium-201 and technetium-99m), representing 80 percent of all *in vivo* studies in nuclear medicine. About one in four patients in American hospitals undergoes an examination with the scintillation camera as part of the process of medical diagnosis. Almost 7000 cameras are now being used in hospitals of all sizes in the United States, and 3000 of these are used in conjunction with computers to enhance the images produced.

**Scanning Instruments** The familiar CAT Scan (Computer Assisted Tomography Scanning) is a vital tool in medical diagnosis, yielding three-dimensional views that reveal body structure in striking detail. However, because CAT Scans cannot depict the active functioning of body organs, there was a further need for a device that could provide such views of regional physiological processes, such as blood flow and metabolism. This led to the development of the PET (Positron Emission Tomography) scan and the use of short-lived radioisotopes of elements that occur naturally in the body (e.g., oxygen, nitrogen, and carbon). Once these radioisotopes are injected and become distributed, their positron emissions are attracted to electrons associated with the normal matter in the body. Both particles are thus annihilated, and a new form of energy is emitted which can be detected by the PET scanner. This information is processed by computer to reconstruct images of the internal distribution and movement of the radioisotope and thus the functioning of the organ of interest. Several companies now manufacture the PET scanner at costs of about \$1 million per unit. This instrument is considered to be enormously valuable in diagnosing and understanding

diseases of the brain (e.g., cancer, mental diseases, epilepsy) and of the heart and lungs.

**Instrument Standardization** Nuclear instruments, including those used in nuclear medicine, are produced by many manufacturers and at one time were not compatible electrically or mechanically. In any new situation it was often necessary either to forego the use of instruments on hand or to replace them with compatible units at considerable cost. Under the nuclear medicine program, a modular nuclear instrument system was developed to provide mechanical and electrical power supply interchangeability. Other compatible modules were designed to feed signals from these instruments to computers and other processors and associated software. These concepts were adopted by standards-setting institutions and manufacturers and have been promulgated worldwide. Annual U.S. sales of the modular and automated systems amount to \$23 million and \$17 million, respectively, and represent 50 to 60 percent of the world market.

## Treatment

**Hyperthyroidism** Hyperthyroidism, characterized by excessive levels of circulating thyroid hormones, can be marked by a variety of clinical conditions, including increased metabolic rate, enlargement of the thyroid gland, rapid heart rate, and high blood pressure. The three major treatments for this condition (surgery, drugs, or iodine-131 therapy) focus on destroying the abnormal thyroid tissue that is producing the excess hormone. Surgery to remove the thyroid gland is painful and expensive and carries risks. The use of drugs requires long-term treatment, incurs possible side effects, and may eventually end in surgery. However, it was found in the early 1940's that the iodine-131 radioisotope concentrates in the thyroid gland, and a means to destroy overactive tissue through short-range particle emissions was thus provided.

The early discovery of this treatment and its selectivity are evident from the fact that, from the mid-1940's to the late 1960's, iodine-131 was the principal radioisotope used in nuclear medicine. For almost 50,000 persons each year in the United States who undergo iodine-131 treatment in place of surgery, the annual savings in terms of productive time and lower medical costs have been computed to be \$280 million.

**Parkinson's Disease** Parkinson's disease, a debilitating neurological disease, afflicts close to one million persons, with 50,000 new cases per year. In two-thirds of the cases, the onset of symptoms occurs between the ages of 50 and 70 and becomes progressively worse. In the early 1950's, several radioisotopes, particularly manganese-56, were used to investigate a possible link between trace metals and this disease. Although no conclusive connection could be made between the disease and manganese poisoning, several new areas of research evolved from these studies. Eventually, it was found that there is a deficiency of an amino acid, dopamine, in the brains of persons suffering from Parkinson's disease and that this amino acid could be synthesized internally after intravenous injection of a related compound, L-dopa. The treatment does not cure the disease but can mitigate the severity of its progression. It produces initial improvement in 50 to 75 percent of the cases, slows the rate of advance of the disease, and decreases the mortality rate. Thus the benefits of this treatment can be measured in terms of improved quality of life (i.e., increased years of work and independence and a decreased or postponed period of incapacity) with an average increase of 2.5 person-years of active or productive time per person afflicted. Based on 50,000 new cases per year in the United States, this translates to a gain of approximately 125,000 person-years of active life annually.

## The Future

This brief account of selected accomplishments over the 40-year program of energy-related health and environmental research only partially illustrates its role in fulfilling an important national need. Use of this style of presentation makes it difficult to convey the program's most important characteristics: an evolutionary, integrated, and multidisciplinary research commitment; a synergism between fundamental science and applied problem solving; and an inevitable share of scientific setbacks as well as achievements. Thus the accomplishments in reality represent a continuum of scientific development—from the basic unraveling of bioenvironmental processes and the coupling of seemingly disparate facts to their application to specific problems.

These program characteristics, in turn, lend a distinct characteristic to the research itself: it is built continually upon an established base of knowledge, the rewards becoming increasingly apparent far downstream of the initial thought and investment. Thus, to a large extent, the program's future accomplishments are already embedded in its studies of the past and the present.

As a part of the evolving national energy mission, a responsive research program has developed the expertise and facilities required for its newer roles. The evolution continues, centered around a long-term commitment to fundamental and basic research, toward addressing problems and issues of a high-risk nature with an anticipatory rather than a regulatory approach. Of particular importance to the future is the fact that the program's multidisciplinary talent and capabilities in unique, dedicated facilities constitute a valuable national resource.

The research program is therefore as well equipped to meet future challenges as it was to meet past challenges. As our energy mission continues to evolve, with changing patterns of energy demand and the accompanying development of

responsive new sources, it is reasonable to expect research contributions to assure safety, acceptability, and compatibility with the national goal. On this point it is significant that atmospheric science and the health effects of chemical exposures (two of the three elements of the energy-related *source-transport-effect* triad) were among the seven research areas recently identified by the President's Science Advisor as likely to return the highest future scientific dividends as a result of incremental federal investments.

The promise for the future therefore lies within the program's traditionally interactive and interdisciplinary approach to complex problems. New biophysical and chemical tools and techniques in biomedical and environmental research now make it possible to attempt unprecedented studies on cells, molecules, and processes relevant to the "triad." These technical advances, applied to basic studies, will continue to contribute to answering energy-related questions, as well as to increasing knowledge about *causes* and *effects* in biological systems. And, as in the search for radiation repair mechanisms which led to discoveries of DNA behavior and important theories of the nature of human disease and its treatment, the program's research will continue to lead in making fundamental and practical contributions in reducing uncertainties on the health and environmental aspects of emerging energy technologies.