THE COVER: Twenty researchers participating in ORNL's Life Sciences/Synfuels Program mark the carbon-hydrogen bonds in the five-ringed benz[a]pyrene molecule, an exemplary organic material in coal-derived products, which are being studied for their biomedical and environmental effects. For a comprehensive overview of this relatively new interdisciplinary program, read the article beginning on page 1.

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OAK RIDGE NATIONAL LABORATORY
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A SPECIMEN OF UNTREATED wastewater and a crude oil sample from one of ERDA's coal liquefaction pilot plants arrive at Oak Ridge National Laboratory. After studying the wastewater sample and identifying many of its constituents, an analytical chemist delivers it to a group of ORNL ecologists, who perform tests to determine whether the effluent is toxic to microorganisms and fish, whether its components get into the aquatic food chain, whether any potentially hazardous constituents are transformed into harmless chemicals by such agents as sunlight and organisms metabolizing them. Effluent material and product oil are sent to ORNL biologists, who test the biological effects of these substances on specific cells and whole animals. Using various separation schemes, a group of ORNL analytical chemists also provide the ecologists and biologists with fractions of the wastewater and crude oil samples—that is, they break them down into acidic, basic, and neutral components. For the biologists, the liquefaction product is further fractionated into compounds with ringlike structures like the polycyclic aromatic hydrocarbons (PAH), into compounds with straight-chain structures (aliphatics), or into organics containing nitrogen or sulfur.

ORNL biologists subject each fractionated oil sample to a battery of tests to ascertain if the substance in question alters the genes of various microbes, human and animal cells, fruit flies, or mice. If the substance is found to be mutagenic in the rapid-screening tests, there is a chance that it may cause mutations and, perhaps, also cancer in man. Positive results raise a red flag. Thus, a series of more extensive, time-consuming mutagenic tests is initiated. The substance is also tested for carcinogenic properties, say, by painting it on the backs of mice and observing if skin tumors are readily produced. The material is further fractionated and tested so that researchers can zero in on the compounds that are biohazards. Tests also
include experiments designed to detect metabolic change of the compounds into potentially mutagenic and carcinogenic chemicals.

ORNL analytical chemists, who have studied wastewater samples from coal-liquefaction facilities, have confirmed others' findings that these samples contain a high percentage of phenolic compounds. Phenols, produced by the carbonization of coal, are aromatic alcohols often found to be tumor-promoting agents—that is, they render cells more susceptible to the action of known carcinogens. In ORNL's Chemical Technology Division, a project is under way to build a better bioreactor in which a special strain of bacteria reduces the phenol content of coal-liquefaction wastewater to environmentally acceptable levels.

In the Health Division of ORNL, hygienists are setting up control procedures and air monitors to minimize coal researchers' contact with potentially carcinogenic substances from coal-conversion experiments, and medical doctors examine the researchers periodically for possible pathological changes in their skin and lungs. All these activities are examples of the multidisciplinary approach of ORNL's Life Sciences Program in Support of Synthetic Fuels.

Program Goals

Nuclear power plants have been in operation in the United States for 20 years, and coal-fired steam plants have been producing electricity since shortly after the turn of the century. But not until the late 1960s have there been coordinated efforts to determine the total effects on human health and the environment of such technologies. Radiation releases, thermal discharges, sulfur-dioxide emis-
As our domestic oil and gas supplies dwindle and our reluctance to depend on foreign sources of energy persists, it is clear that Americans need to meet future energy demands by relying increasingly on our most abundant fossil fuel, coal. Endowed with 3 trillion tons of coal beneath our continent, we have the potential for producing much of our fuel gas and fuel oil by subjecting coal to various conversion processes. In an era when production of energy is no longer permitted to jeopardize the environment, coal conversion is specifically mandated to yield clean fuel from coal. Thus, production of synthetic fuels is an environmental technology. Now in its embryonic stage, the technology is being developed to minimize production and discharge of potentially toxic chemicals. Process engineers at coal-conversion pilot plants are receiving constant feedback from researchers of various disciplines at ORNL and elsewhere on potential biomedical and environmental problems posed by a particular process. Like a team of doctors diagnosing genetic defects in a fetus and then correcting the problems in utero, engineers, chemists, and life scientists from all over the nation are collaborating to give birth to a vital technology that will move us closer to energy self-sufficiency. It is not inconceivable that the United States, by the year 2000, may have as many as 40 commercial-size synfuel plants consuming a million tons of coal a day and employing 150 thousand persons. ORNL is playing an important role in bringing coal-conversion technology to fruition and guiding its safe development. One aspect of this role is the work of the Life Sciences in Support of Synthetic Fuels Program coordinated by Carl Gehrs and reported in depth in the following article by Carolyn Krause, shown here interviewing Gehrs.
ORNL can marshal specialists in various scientific disciplines and combine them with the appropriate administrative skills to plan and begin to implement a program of this magnitude in a relatively short time. This cannot be done in most institutions and is an example of the vast capabilities within the ERDA multidisciplinary laboratories."

“One of our achievements,” Gehrs says, “has been the development of a systematic integrated research approach to address the questions of coal conversion. We served as the lead laboratory in developing a Balanced Program Plan, which describes coal-conversion technologies and recommends what biomedical and environmental research is needed to support the coal-conversion technologies on a national basis.”

The Life Sciences/Synfuels Program covers these areas: (1) chemical and physical characterization and monitoring of coal-derived products and effluents; (2) biological characterization and health effects of these substances; (3) environmental transport and effects; (4) environmental control technology; and (5) assessment. A related effort not part of the program is a project in the Energy Division also dealing with assessment and siting of coal-conversion plants.

The Analytical Chemists

The Analytical Chemistry Division’s Bioorganic Analysis Section under Mike Guerin has a long history of characterizing complex mixtures like condensed tobacco smoke. Its newest challenge is to characterize and prepare for biological tests the different mixtures produced and discharged from coal-liquefaction as well as other energy-related pilot facilities. These early coal-liquefaction products include three potentially carcinogenic classes of compounds—PAH, sulfur-containing heterocyclics, and aromatic amines. The chemists have analyzed wastewater samples and products from shale-oil-retorting and coal-conversion pilot plants at ERDA’s Laramie Energy Research Center and Pittsburgh Energy Research Center, respectively, and from the petroleum-refining industry.

Among the preliminary findings of the chemists are these:

- There were 2 to 10 times as high concentrations of PAH in pilot-plant coal oil as in the shale oils and petroleum, and at least 10 times the concentration of PAH in the tested coal-derived liquids as in tobacco-smoke condensate.

- There were as many as 150 to 200 easily detectable PAH in the coal-liquefaction products, including benzo[a]pyrene (BaP), an important carcinogen.

- Evidence has been found by Wayne Griest for 3-methyl cholangthrene (a compound known to be more carcinogenic to animals than BaP) in product materials from a coal-conversion process being developed for making chemical feedstocks needed for the plastics and chemicals industries. (C.-h Ho is now trying to confirm Griest’s findings.)
Bobbie Brewen inspects fruit flies (Drosophila) for such genetic damage as altered eye color. These insects are the offspring of flies that were exposed to coal-derived chemicals.

- Coal-derived effluents contained a high percentage of phenols, whereas oil-shale-derived effluents were high in relatively innocuous carboxylic acids.

The analytical chemists use a combination of techniques—including solvent extraction, liquid and gas chromatography, and mass spectroscopy—to identify and quantify classes of compounds found in coal-derived mixtures. After the chemists obtain organic concentrates from wastewater samples, they separate them into acidic, basic, and neutral components. The acidic fractions contain phenols and carboxylic acids; the basic fractions, aromatic amines; and the neutral fractions, PAH. The fractionated materials are then further resolved into their constituent compounds by liquid and gas chromatography. Element-selective detectors are used to find, say, compounds containing sulfur (thiophenes) or nitrogen (amines). The chemists have found that it is possible to perform a direct analysis of aqueous coal samples with a commercially made gas chromatographic column packing material. This technique separates the complex sample into individual compounds, which are displayed as peaks on a recorder trace. In one such analysis, 23 compounds were identified.

Bruce Clark is leading an effort to develop techniques for separating compounds from complex coal-derived mixtures without altering the compounds. He is working with Russ Jones to develop a gentle chromatographic separation method, which holds the promise of semiautomation and is less likely to produce artifacts in the samples. The new technique separates chemical compounds by washing them with a solvent down a column of Sephadex beads. Each compound moves down at a characteristic rate because it differs in its strength of adhesion to the column beads, and chemically similar compounds emerge closely together from the column, where they are collected, one at a time, and identified.

Clark is also working to establish at ORNL a repository for samples from various nonnuclear energy processes to be used for research.

In the toxicity and mutagenic screening studies, the analytical chemists interact with biologists, ecologists, and chemical engineers.

Guerin says that other accomplishments of his division include:

- Collaborative development and validation of a chamber for experimental exposure of plants to gaseous effluents;
- Trace-element characterization of aqueous materials related to synfuels;
- Preparation and characterization of PAH isolates (neutral fractions enriched in PAH) from synfuels;
- Identification of constituents of the highly mutagenic basic fraction of a syncrude; and
- Quantification of PAH and paraffin constituents of crude oils and aqueous by-products.

**Screening: the Biologists**

ORNL biologists work closely with the analytical chemists to pinpoint those constituents of synfuel products and effluents that are responsible for biological activity—the ones that are cytotoxic, mutagenic, carcinogenic, and/or teratogenic. The analytical chemists supply the
Jennifer Young counts yeast colonies as part of a battery of tests to determine whether a coal-derived substance is mutagenic.

Biologists with whole and fractionated materials that they have characterized. Biologists, working under the direction of Jim Epler at the new Mutagenesis Testing Facility (Building 9769 at the Y-12 Plant), subject these materials and model compounds representing known constituents of these materials to rapid-screening tests to determine their mutagenic potential.

A rapid, inexpensive method of screening compounds and mixtures for mutagenic effects is exposure of them to microbes. Epler's group conducts bioassays using strains of *Salmonella, E. coli* (bacteria commonly found in the digestive tract), and yeast (one-celled fungi). The quickest screening test utilizes a mutant strain of the *Salmonella* bacteria developed by Bruce Ames of the University of California at Berkeley. The genes of this strain have been modified so that it is incapable of making the amino acid histidine essential to its growth. If the test compound is mutagenic, the exposed *Salmonella* bacteria will revert to their normal state and begin growing without a histidine supplement. The larger the revertant colony counts, the more mutagenic the test chemical is rated. The chemical can also be tested in the *E. coli* and yeast systems.

Ti Ho and Carroll Nix are performing further tests to determine if the suspect mutagen causes chromosome damage in human leukocytes and genetic defects in fruit flies. The microbial mutagenicity assays of fractionated coal-conversion products are performed by groups led by T. K. Rao and Frank Larimer.

Says Epler: "In addition to PAH, we have found that certain quinolines (nitrogen heterocyclics) and a number of aromatic amines are mutagenic, suggesting that they should be tested for carcinogenicity. However, we have determined that a long list of compounds, including phenols, are nonmutagenic and therefore probably not carcinogenic. However, they could have toxic effects or be tumor promoters." Epler's group, using rapid-screening techniques that produce answers in two days to four weeks, has shortened the list of compounds that require examination by expensive, time-consuming mammalian tests.

If a known carcinogen like BaP is not found to be mutagenic in the Ames *Salmonella* system, then a "metabolic activation" test is initiated to determine if the chemical is metabolized into mutagenic (and probably carcinogenic) compounds. In this test, an enzyme preparation from a
liver excised from a rat is added as a reagent to the genetic-screening assay. This enzyme is produced in large quantities by injecting the rat with inducers, thus stimulating the liver to elevate its activity in making a particular enzyme for metabolizing PAH such as BaP. ORNL biologists found that BaP, when "metabolized" by the enzyme added to the Ames assay, is converted into compounds that are mutagenic to the mutant Salmonella.

To determine the risk to man of compounds found to be mutagenic in rapid-screening tests, it is necessary to study the effects of these compounds on mammalian cells and in whole mammals such as mice. Abe Hsie of the Biology Division has been using mammalian cell systems to screen for the mutagenicity and carcinogenicity of energy-related pollutants. The system will detect gene mutations in cultured CHO (Chinese hamster ovary) cells. Hsie has been successful in adding metabolic activation of potential mutagens to this test.

Liane Russell has developed a promising test for mutations in somatic cells in vivo which uses small samples of mice and determines within five weeks whether test chemicals are likely to have mutagenic effects in whole animals. Using model compounds and crude mixtures from liquefaction products in a dose range that is not toxic enough to be fatal, she can inject the test material into pregnant mice, thus exposing embryos in utero to the suspect mutagenic agent. If a mutation occurs in a cell whose (cellular) descendants will specialize in producing pigment, the newborn mice affected will soon grow fur with oddly colored spots; an otherwise black mouse, for instance, might show patches of brown hair. This new "spot" assay promises to save biologists time and money in screening chemicals that may be mutagenic to mammals.

G. A. Sega and R. B. Cumming are trying to detect which compounds in coal-derived materials damage DNA of mouse germ cells following in vivo exposure. DNA, or deoxyribonucleic acid, is the molecular basis of heredity.

Although some of these various tests can perform a screening function, they do not in themselves provide the critical information on
A scanning electron micrograph of Tetrahymena pyriformis exposed to 100 ppm phenol for 3 min. The animals become distorted in shape, their membranes rupture, and their protoplasm is exuded. X 1650.

which an assessment of potential hazard to man must be based. For that assessment, it is necessary to check for genetic damage transmitted to descendants following administration of the chemical to whole animals. Thus, transmissible chromosome aberrations induced in mouse germ cells are used by W. M. Generoso to determine this type of hazard from hydrocarbons and heavy metals associated with nonnuclear energy technologies. The induction of transmitted gene mutations is investigated by W. L. Russell, who uses the specific-locus method on mice exposed to those coal-derived substances to which man is likely to be exposed. Both tests are more expensive (in time and animals) than the other tests and, therefore, limited to substances deemed most hazardous by the screening tests.

Jim Regan is looking for mutagenic effects of model compounds on normal human cells and mutant human cells that are deficient in the ability to repair damage to DNA. He is trying to determine to what extent human cells can repair damage inflicted upon them by coal-derived substances.

Two cell biologists are doing toxicity studies, which have begun yielding results. Terry Schultz and Jim Dumont have been examining the toxicity of synfuel aqueous effluents at the cellular level using protozoa called Tetrahymena pyriformis, an organism selected for study because it proliferates rapidly, can serve as an indicator organism since it abounds in most aquatic environments, and is inexpensive and well studied. The researchers have been looking at the cellular effects of various aqueous samples on this pear-shaped, one-celled organism by monitoring motility and shape, oxygen uptake, and population growth and by examining the ultrastructure with scanning and transmission electron microscopes to determine which organelles in the cells are targets of the toxin.

Samples from laboratory-scale and pilot-scale gasification, liquefaction, and shale-oil-retorting plants have been characterized by the Analytical Chemistry Division and provided to Schultz and Dumont for cytotoxicity studies. They have determined relative toxicity of an array of substituted phenols, known to occur in pilot-plant effluents. Schultz and Dumont have observed that the lethal effects stem from ruptured cellular membranes (the cells’ outer “skin”) and that the sublethal effects of the phenols include reduced respiratory rates and changes in the shape of the mitochondria (cellular organelles, or “powerhouses,” that produce energy for the cells through respiration). They have also determined that the most toxic phenols have the greatest affinity for the lipids and proteins making up the cellular membrane and are the least soluble in water.

Dumont has found that very low concentrations of phenols will cause abnormal development of frog tadpoles, rendering them unable to survive and reproduce in normal environments. He is also studying the teratogenic effects on developing tadpoles of heavy metals like selenium, cadmium, and arsenic (which are also present in synfuel effluents).

Cancer Research

Workers in coal-conversion plants may come in contact with liquid products or aerosols either during routine maintenance or following accidental spills or inadvertent releases. The general public may be exposed if coal-derived petroleum substitutes are used as lubricants, fuels, or petrochemicals. In both situations, it is considered imperative that a given technology produce a
While Larry Gipson holds the mouse, June Whitaker uses a micropipette to administer a known quantity of a test chemical to the animal’s shaved back. If the test chemical is carcinogenic, the mouse will eventually develop skin tumors. These measured doses are delivered to the mice three times a week as part of the skin painting carcinogenicity experiment now under way in the Biology Division.

clean product and that accidental in-plant exposure be minimized or eliminated if possible.

A number of researchers in the Biology Division are developing rapid in-vitro bioassays to be used to predict and quantify the carcinogenic potency of coal-liquefaction products themselves and effluents produced during their manufacture. Studies led by Paul Nettesheim are directed toward understanding early changes in respiratory lining cells which may forecast exposure to an environmental or industrial carcinogen. Frank Kenney is coordinating research to detect molecular changes that are specific and predictive of eventual tumor formation. These studies and other novel bioassays must eventually be evaluated against the empirical standard of actual tumor induction in the whole animal, using the same compounds for both short-term test-tube and long-term animal tests. Only by direct comparison of test results will experience be obtained to allow substitution of short-term cellular or molecular bioassays for traditional whole-animal carcinogenesis trials.

To provide this reference data, Mike Holland and his colleagues are conducting a series of dose-response experiments in 1600 mice. Groups of 50 (25 male and 25 female) are exposed to known quantities of two coal-liquefaction products, a
shale oil, and a blend of natural petroleum supplied and characterized by the Analytical Chemistry Division. All compounds are diluted in the same solvent and applied at four dose levels directly on the skin, three times each week. Exposure continues until all mice in the group have developed one or more tumors or until 24 months have elapsed, whichever occurs first. Because human skin and mouse skin are sensitive to tumor induction after exposure to coal-conversion products, and because the tumors in both man and the mouse appear similar and behave in a similar way, it is likely that a compound proven tumorigenic in the mouse will also be active in man.

Coal tar is one of the oldest known substances used to produce skin tumors in animals for experimental purposes. Eventually, an active fraction was isolated from coal tar and on further analysis was found to contain PAH. Knowledge that coal tar contains known carcinogenic PAH leads inevitably to the question: Can activity of a complex hydrocarbon mixture be estimated by measuring the amount and kind of PAH present? In an effort to answer this question and at the same time obtain dose-response and potency data, Holland and his colleagues are exposing mice to this mixture and combining its diluted isolates. By comparing the tumor response of the diluted unfractionated materials (that have been isolated, then it should be possible to distinguish between differences due to non-PAH components from differences due to composition. If different potencies are observed among the separate isolates, then it is probable that differences in specific PAH, unique to each starting material, account for differences observed between the unfractionated and diluted source materials.

In another cancer research project, Jim Regan and Ray Waters have found that 4-nitroquinoline oxide, a potent carcinogen produced by coal conversion, is much more likely to transform rat cells into cancerous cells if these cells are first infected with a leukemia virus. The virus appears to be acting as a co-carcinogen, reducing the ability of the cellular DNA to repair itself and therefore rendering the cell more susceptible to the action of the coal-derived carcinogen.

**Screening: The Ecologists**

Control engineers at coal-conversion plants need to know the nature of plant wastes so they can decide whether to modify their waste-control systems to provide more adequate treatment of the effluents. One of the purposes of the Synthetic Fuels Program in ORNL's Environmental Sciences Division, according to Carl Gehrs, program manager, is rapid identification of the materials that deserve a closer look as to their environmental behavior and effects. ORNL ecologists are screening coal-conversion effluents from pilot plants for toxicity. More than half of the organic constituents of such wastewater are phenolic compounds, which are very toxic chemicals. Fortunately, phenols are not expected to pose a major waste-treatment problem because they can be removed rapidly by microbial degradation. Improving methods of biological treatment of effluent containing phenols is being studied by ORNL's Chemical Technology Division and will be discussed below. Environmental researchers have been examining the relative toxicity of untreated and treated coal-conversion effluent from ORNL and elsewhere to determine how effective waste-treatment processes are.

For some of the ecologists' studies, the Analytical Chemistry Division provides whole effluents and effluent fractions—organic concentrates broken down into acidic, basic, and neutral components and then diluted. Various aquatic organisms (*Daphnia* water fleas, fathead minnows, other zooplankton, bluegill fish) are then exposed to the effluent samples, and their death rates are used as an indication of toxicity. It has been observed that a fraction representing only a small percentage of the effluent may be many times as toxic as a larger fraction of the same effluent. Some of the tentative results of the toxicity studies are:
Gehrs, Ben Parkhurst, and Jenny Forté have found that the untreated effluent from a pilot plant employing the COED (Char Oil Energy Development) conversion process was about twice as toxic as the effluents from a shale-oil-retorting facility and from the Synthane coal-conversion pilot plant (operated by ERDA's Pittsburgh Energy Research Center).

Using zooplankton, they have also demonstrated that fractions of ether-soluble weak acids, which contained the phenols known to be highly toxic, were 20 to 30 times as toxic as fractions of ether-soluble strong acids and of water-soluble strong acids, respectively.

By doing a comparative study of the toxicity of treated and untreated effluents consisting of a standardized phenolic feed and a hydrocarbonization scrubber water, Ben Parkhurst found that the treated effluents in which phenolic concentrations were considerably reduced were still extremely toxic to bluegills and zooplankton. He concluded that the treated effluent contained some toxic material (other than phenols) that either had not responded to treatment or possibly had been produced as a by-product of the treatment.

Chemical analysis of the effluent studied by Parkhurst indicated that high concentrations of ammonia were still present even after treatment. (Ammonia is a coal-conversion waste product, a small amount of which serves as a nutrient for the bacteria that consume phenols as part of the treatment process.) Since ammonia is known to be highly toxic to aquatic organisms, Parkhurst postulated that ammonia was the cause of the residual toxicity. Doug Lee of the Chemical Technology Division, who helped develop the fluidized-bed bioreactor to treat phenol-containing effluents, suggested dialyzing the effluent to remove the ammonia. “Toxicity tests on the dialyzed effluent have produced no mortality to fathead minnows exposed to a 30% dilution of the effluent nor to zooplankton exposed to 100% effluent for 96 hr,” Parkhurst says. “These results appear to confirm that ammonia is the toxic agent still present in the effluent.”

ORNL ecologists are trying to ascertain which elements present in coal-conversion effluents are toxic to freshwater organisms or could be accumulated in aquatic biota to levels not safe for human consumption. Approximately 50 trace elements were identified in coal and are thus suspect as possible contaminants in process effluents. After Joel Carter of the Analytical Chemistry Division detected measurable concentrations of 30 of these elements (using spark-source mass spectrometry) in aqueous process streams from the COED process, ecologists Steve Hildebrand and Bob Cushman determined that 19 elements possess a toxicity and/or bioaccumula-
tion hazard potential in aquatic ecosystems. The elements they found that have both a high potential toxicity and potential bioaccumulation hazard are chromium, iron, nickel, lead, and zinc.

To facilitate the assessment of the potential hazard of these elements, Cushman and Hildebrand, along with Rod Strand and Regina Anderson of the Environmental Sciences Division's Data Resources Program, compiled existing information on trace-element toxicity to aquatic biota into a computer-searchable data base. It was found that the toxicity of many of the elements had been little studied. To begin filling some of the gaps, Hildebrand and Cushman tested the effect of known concentrations of gallium and beryllium on the hatchability of carp (Cyprinus carpio) eggs in the laboratory. For comparison, they also tested copper, an element whose toxic effects have been well described. Beryllium was found to be about as toxic as copper, but gallium was an order of magnitude less toxic to the carp eggs.

Since coal-conversion effluents also include airborne particulates and gases, ORNL ecologists are studying the effects of gaseous effluents on vegetation. Dave Shriner and Sandy McLaughlin have been investigating the effects of exposing red kidney bean seedlings to benzene, a representative aromatic compound. They collaborated with Art Horton of the Analytical Chemistry Division, who developed the gas-metering and monitoring system for the exposure chamber used in the experiment. Since no deleterious effects on growth, yield, or photosynthetic rates were found following exposures at levels equivalent to the peak occupational exposure limits set by the EPA, they concluded that it is "highly unlikely that benzene alone will cause acute or chronic injury to terrestrial vegetation in the vicinity of coal-conversion facilities." But they also found that single, one-hour exposures of the kidney bean seedlings to levels of carbonyl sulfide within an order of magnitude above expected average ground-level concentrations caused a decline in photosynthesis—the ability of the plants to synthesize carbohydrates in the presence of sunlight. When low-level exposure to the gas ceased, however, the plants recovered their photosynthetic capacities within three days (the shorter and lower the exposure, the faster the recovery).

What effects do interactions of trace amounts of organic compounds in treated coal-conversion effluents have on the toxicity of any particular constituent? This question was studied by Steve Herbes and J. J. Beauchamp of the Computer Sciences Division. Since phenols and aromatic amines are the most toxic compounds identified so far in pilot-scale effluents, they examined potential toxic interactions between resorcinol (a phenol) and 6-methylquinoline (an aromatic amine) to the zooplankton Daphnia magna to determine whether such interactions may be important in natural water systems. Finding that mixtures of the two compounds were significantly less acutely toxic than either one alone, they concluded that "toxic effects of effluent mixtures may be more complex than simply the summation of the individual toxicities of the constituent chemical classes."

Tracking Down Effluent Components

"The second aspect of our program," Gehrs says, "is concerned with understanding the mechanisms of effect, persistence, fate, transformation products, and food-chain kinetics of effluent components. Our efforts will eventually provide the data bases necessary for assessing and predicting the potential implications of a coal-conversion economy."

What the biologists learn about the potentially hazardous effects of certain coal-derived compounds, Gehrs notes, will be especially meaningful if the ecologists determine that those compounds are likely to get into the critical pathways leading to the air breathed by man and the water and food ingested by him. ORNL ecologists are particularly interested in the wastewater from coal-conversion plants; they are trying to determine which constituent compounds of these effluents are most likely to pose environmental problems. As a result of a literature survey, Herbes, George Southworth, and Gehrs have selected for study three major classes of compounds anticipated in aqueous coal-conversion effluents which could enter the critical pathways and threaten human health. They are PAH, aromatic amines, and thiophenes.

Although they are moderately nontoxic, all three groups may include compounds that are carcinogenic and mutagenic. They are all resistant to microbial degradation and therefore are not easily removed from wastewater by biological treatment. And they are all bioaccumulable—that is, they are concentrated to high levels in aquatic
organisms (including those eaten by fish) and may eventually be transported to man through the ingestion of contaminated fish and shellfish.

The ecologists are trying to ascertain what happens to PAH when they enter wastewater. Do some become dissolved? Do most adhere to wastewater particles which transport them? How rapidly are they broken down by light? What happens to dissolved PAH or to PAH sorbed to particulates when they are consumed by aquatic organisms? How much is retained in the organisms? How much is excreted unchanged or excreted after being transformed by metabolism? Are the excreted metabolites themselves hazardous?

Using representative PAH compounds, Herbes and Southworth have studied sorptive partitioning—that is, the extent to which various PAH compounds are dissolved in effluent or sorbed on wastewater particulates. By inoculating carbon-14-labeled PAH ranging from two to five rings with samples of biologically treated wastewater, Herbes and Southworth found that significant fractions of PAH may be present in both dissolved and particulate forms. They demonstrated that sorption increases with molecular size, decreasing water temperature, or increasing suspended-solids loading. In particular, they observed that, whereas naphthalene is found almost entirely in soluble form, 30 to 40% of benz[a]anthracene and BaP may be present in biologically treated wastewater effluents in particulate form.

Herbes and Southworth also investigated the tendency of PAH and aromatic amines to accumulate in early links in the aquatic food chain. Their results indicated that the components of higher molecular weight (which include most of the known carcinogenic PAH compounds) were rapidly concentrated several thousand times over by zooplankton (Daphnia pulex). Higher organisms feeding on zooplankton from contaminated waters, they concluded, might receive a significant input of carcinogenic material from this source, possibly posing a hazard to people eating fish.

Could PAH compounds be eliminated by microbial alteration and ultimate degradation in sediment in natural waters? Herbes and Linda Schwall have determined rates of microbial action on test compounds by incubating tagged PAH with sediment samples in vials. They then used column chromatography to separate PAH alteration products from residual PAH in oil-contaminated samples. Their results: "While two- and three-ring compounds are altered within hours, benz[a]anthracene and BaP are altered extremely slowly." Their conclusion: "Carcinogenic PAH can thus be anticipated to accumulate in sediments below source outfalls and cannot be degraded even by acclimatized microbial populations."

When zooplankton feed on coal-conversion wastewater particulates to which carcinogenic PAH compounds adhere, is a significant portion of these PAH retained in the organism or transformed through metabolic alteration into benign compounds that are excreted? Herbes and George Risi studied this question after having demonstrated the ability of several invertebrates to concentrate anthracene, a three-ring PAH compound, apparently from both dissolved and particulate forms. They examined the kinetics of excretion and metabolic alteration of anthracene by Daphnia pulex, a representative zooplankton, to evaluate the effect of excretory processes on the potential for bioaccumulation of PAH compounds in aquatic organisms.

They found that the zooplankton altered a fraction of the tagged anthracene used in the experiment. But they also observed that the rate of metabolite excretion is very small in comparison with the transfer rate of unaltered anthracene. Hence, they concluded that metabolite excretion decreases only slightly the 14C-anthracene body burden of the animals. Says Herbes:

"Although Daphnia pulex are able to metabolize PAH compounds, the rate of metabolic excretion is likely to be insufficient to inhibit bioaccumulation by several hundredfold factors, primarily because uptake of PAH by Daphnia is extremely rapid. A significant potential for biocentration of the compounds by fish through zooplankton predation therefore exists. The rate of metabolism of PAH compounds by marine fish is more rapid than that by Daphnia and may be more similar to the rate of uptake; metabolic elimination would then have a greater effect on net bioaccumulation by fish. Metabolic alteration of PAH by zooplankton may be more ecologically important as a mechanism of net degradative removal of PAH from natural waters than as a mechanism for prevention of biomagnification of the compounds within aquatic food webs."

Since large quantities of solid wastes will be generated from coal-conversion facilities and require disposal, information on the leachability
G. B. Dinsmore, technician, examines a fluidized-bed bioreactor, a tapered column containing coal particles with bacteria on them that effectively and relatively quickly reduce phenolic compounds from coal-conversion waste streams. Recent studies have shown that, despite removal of phenols, the treated effluents had a residual toxicity, which was found to be caused by the presence of ammonia. Subsequent dialysis of the effluent removed the ammonia, making the treated wastewater environmentally acceptable.
of waste constituents is needed for the design of the most efficient disposal schemes. Tsuneo Tamura, who seeks through his research to define the characteristics of coal-conversion solid wastes and provide scientifically sound options for treatments that would minimize adverse impacts on the environment, is currently conducting leaching experiments on solid wastes using batch and column techniques. He will analyze leachates for soluble and particulate components, including toxic substances.

Cleaning Up Wastewater

A novel bioreactor developed in ORNL's Chemical Technology Division for removing nitrates from nuclear fuel reprocessing wastes has dramatically reduced the concentrations of highly toxic phenols in aqueous effluents from coal-conversion processes. The fluidized-bed, tapered-column system has taken waste-stream samples containing more than 200 parts per million of phenols and reduced these concentrations to 10 parts per billion (ppb)—an environmentally acceptable level, although drinking water must not contain more than 1 ppb phenol to comply with EPA standards. The system uses a mixed culture of Pseudomonas type bacteria (attached to small anthracite coal particles), which consume phenols and convert them to harmless material. The effect is well known in the coking industry, which uses the bacteria in activated-sludge ponds to treat its phenol-containing wastes.

Doug Lee and Chuck Hancher are testing the relative rate at which the bioreactor can treat phenol-containing wastes, including effluents from ORNL's test hydrocarbonization reactor. They have found that it can treat equal volumes of wastes five times as fast as packed-bed bioreactors and ten times as fast as activated-sludge ponds. The limiting factor is the rate at which oxygen can be delivered to the aerobic microorganisms. The bioreactor offers such advantages over packed-bed reactors and sludge ponds as lower pumping costs; continuous operation; and improved mixing characteristics, as the constantly agitated bacteria adhering to the suspended coal particles have better contact with the upward-circulating phenols. Because of these advantages, there is considerable commercial interest in this novel bioreactor concept.

According to Wilson Pitt, program manager for biotechnology and environmental programs in the Chemical Technology Division's Advanced Technology Section, the bioreactor will also be used to find out whether other species of microorganisms can effectively remove PAH, aromatic amines, and other problem materials in coal-conversion effluents. This year, ORNL ecologists have been working with the bioreactor researchers to determine which constituents, other than phenols, pose a toxicity problem in treated effluents. Pitt and Bob Jolley of the Chemical Technology Division are trying to identify the pollutants in effluent streams before and after they are treated in the bioreactor. As stated earlier, preliminary results indicate that residual quantities of ammonia are responsible for the toxicity of the treated effluent.

Chemical engineers at ORNL are also studying other methods for removal of PAH from coal-conversion wastewater. Since PAH have a strong tendency to adhere to solids, ORNL engineers are studying the possibility of removing PAH by circulating the effluent through a column packed with organic polymer materials with a high surface area.

Jerry Klein and Ray Barker have completed an assessment of aqueous wastes expected from the hydrocarbonization process. Their report identifies which in-plant process streams contain hazardous materials that could pose environmental problems through normal or accidental releases. In the absence of emission standards for coal-liquefaction plants, Klein and Barker have referred to coking industry standards to make educated guesses, for possible guidelines for liquefaction plants. They discuss what available and potential technologies could be applied to modify the process and improve waste treatment to minimize the threat of aqueous effluents to the environment.

Human Health Impacts

Processes currently used for converting coal to liquid or gas products may subject workers to such chemical and physical stresses as PAH; phenols and cresols; sulfur compounds; toxic trace elements present in coal (such as mercury, arsenic, selenium, and cadmium); coal dust; and noise and heat stress. Exposure to PAH is the most difficult for industrial hygienists to control and generates greatest concern because of their cancer-causing potential.
George Oswald, an engineer who works at the hydrocarbonization pilot plant, is wearing the required protective clothing and a respirator to minimize contact with potentially hazardous chemicals. Researchers use the pilot plant to test a pyrolysis process in which a fluidized bed of coal, subjected to elevated hydrogen pressures, reacts to produce hydrocarbon liquids, a residual char, and gases that contain methane, hydrogen, carbon oxides, and other light hydrocarbons. Among the potentially hazardous chemicals produced in this liquefaction process are PAH, which are condensed unsaturated, ring-shaped molecules composed of carbon and hydrogen.

Studies of coke-oven workers in the steel industry have revealed an increased incidence of cancer of the lung and genito-urinary system in these employees; this phenomenon has been attributed to the presence of carcinogenic chemicals such as PAH at very high concentrations in airborne particulates in the workers' environment. In the 1950s, when Union Carbide Corporation set up its experimental coal-hydrogenation unit at Institute, West Virginia, industrial hygienists recognized the carcinogenic potential of chemicals produced by coal conversion. Using experimental animals, Mellon Institute in Pittsburgh studied Carbide's product streams and identified the points in the process where the intermediate streams were found to be carcinogenic.

Based on Union Carbide's study at the coal-hydrogenation unit, ORNL has developed an industrial hygiene and medical surveillance program which has become a model for industrial and government facilities using coal-conversion processes.

**Industrial Hygiene at ORNL**

ORNL's Industrial Hygiene Department, directed by Newell Bolton, has been in existence since 1961, but has acquired a much higher visibility among Chemical Technology Division employees since the establishment of the Coal Technology Program in 1974. A new employee doing coal-conversion research soon becomes acquainted with ORNL's industrial hygienists, who brief him on the possible hazards of his work and provide him with a Health Division brochure written by the Industrial Hygiene Department. The new employee learns about the Department's monitoring procedures, which include air sampling in areas where research in both coal conversion and the carbon coating of uranium fuel pellets is conducted. Hygienists sample the air to make sure that the concentration of airborne particulates known as coal tar pitch volatiles (CTPV) does not exceed 0.2 milligrams per cubic meter. (Studies have shown that there is no significant increase in internal cancers in coke-oven workers if CTPV concentrations are kept within this limit.) CTPV particulates collected by hygienists are evaluated by analytical chemists to determine if the particulates contain the carcinogen BaP.

If the new employee works with equipment contaminated with PAH, he will be required to wear protective clothing, to put on a respirator to prevent inhalation of coal-derived particulates, and to rub barrier cream on his skin to minimize skin contact with hazardous substances. Skin surveillance involving the shining of ultraviolet light on workers' skin is used only when there is a real probability that the skin will be contaminated with coal "oils." (It is not used routinely because of the potential carcinogenic effect of uv light in prolonged exposures). If the employee's skin has unusual fluorescent spots, it is an indication that PAH have gotten on his body, since many PAH fluoresce strongly under uv light. Workers are cautioned to avoid skin contact with...
PAH. Careful washing with soap and water will remove most of the contamination. According to Bolton: “We’ve detected only two or three marginal cases of potential skin contamination. Simple washing removed the material from the skin.”

Bolton says that his Department will be studying the effectiveness of new barrier creams and of the laundering process for protective clothing (in light of a 1972 study of Czech coke-oven workers that showed a buildup of BaP in the workers’ protective clothing despite what was thought to be adequate laundering). Bolton and his colleagues are also investigating alternatives to uv light for skin examination.

The hygienists are surveying about 80 employees in the Coal Technology Program who are involved directly or indirectly with experiments in which there is a potential for skin contact with potentially hazardous liquid products.

**Medical Surveillance**

ORNL’s Health Division gives each new employee in the Coal Technology Program a physical examination supplemented by a special evaluation of the skin and a sputum cytology test. Dr. C. L. Huddleston, a consultant in dermatology from Knoxville, examines the skin to detect changes that may be related to work exposure. Coal technology employees receive a sputum cytology test before beginning work and at yearly intervals to detect any abnormal changes in cells shed by the lung into the sputum. Sputum samples are sent to Dr. Geno Saccomanno of St. Mary’s Hospital in Grand Junction, Colorado, who performs the cytology work. Dr. Tom Lincoln, director of ORNL’s Health Division, calls Dr. Saccomanno one of the best cytologists in the world because of his skill in detecting subtle alterations in sputum cells which indicate a degenerative change in the cells’ nuclei and cytoplasm that could eventually lead to cancer. The condition of all ORNL employees’ lungs is also monitored by x rays at 18-month intervals.

This type of medical surveillance program is needed in the coal-conversion industry as well as in research facilities, Dr. Lincoln says, even though threshold limits have been set for CTPV and BaP in working areas. Dr. Lincoln, who for many years has examined workers exposed to low-level radiation, spoke on the need for medical surveillance at one of the ORNL-sponsored “Workshops on Exposure to Polycyclic Aromatic Hydrocarbons in Coal Conversion Processes” held March 9-11, 1977. Says he:

“Medical surveillance is needed because threshold limit values are based on particulate concentrations in the air and do not account for possible absorption through the skin and ingestion through the mouth. Another problem is that some people are more susceptible to the action of carcinogens than are others.

“People who smoke are more susceptible. For example, it was found that there was a fantastic increase in lung cancer among smokers working in the asbestos and uranium-mining industries, whereas there was only a slight increase in cancer among nonsmokers doing these jobs. Blonds and redheads have a much higher incidence of skin cancer, but blacks rarely get skin cancer. Exposure to sunlight may accelerate the appearance of cancer in people who are also exposed to carcinogens, as in the coal-conversion industry.”

In summarizing the concerns of the people who monitor the health of workers in the coal-conversion industry, Dr. Lincoln says:

“Although every possible effort will be made to keep exposures as low as possible, it may be impossible to prevent some low-level exposures in pilot plants. Hence, epidemiologists must try to follow the people in pilot-plant operations to determine whether there is an increase in the incidence of these cancers. We are roughly in the position that the radiation industry was in in the 1940s. Without a careful epidemiological study, a small increase in cancers of the skin, lung, and urinary tract will get completely lost in the ‘noise’ of the normal incidence. Being eventually able to say with confidence that there has been no increase should be of great value to a burgeoning new industry.”

**Monitoring Workers**

In the nuclear industry, workers for years have worn personal radiation monitors that chirp and flash in response to rising radiation levels. No such personal monitors are currently available for workers in coal-conversion pilot plants, but an effort is under way at ORNL and elsewhere to develop and evaluate instrumentation to alert workers to the occurrence of leaks, to detect skin contamination, and to indicate effectiveness of decontamination measures.

Dick Gammage and his coworkers in the Assessment and Technology Section of the Health
Physics Division have been studying whether they can modify available instrumentation and develop new techniques for use by industrial hygienists in monitoring coal-conversion workers. For example, they have tested an ultraviolet absorption spectrometer at ORNL's hydrocarbonization pilot plant (under Hank Cochran) and found it suitable for detecting aromatic vapors such as naphthalene. Alan Hawthorne is modifying the instrument so that it can detect and measure a number of PAH in gaseous and liquid samples. The ultimate aim is to make a simple, portable instrument fitted with a microcomputer that can provide industrial hygienists with rapid information on contamination levels.

Tuan Vo-dinh, who helped develop room-temperature phosphorescence at the University of Florida, is applying this technique to measurements of air and liquid samples. John Thorngate is developing a thermoluminescence system to irradiate PAH samples at low temperatures with low-energy electrons and to measure any thermoluminescence that occurs as the samples return to room temperature (each compound has its own characteristic luminescence). Gammage's group has also studied the cost, availability, and effectiveness of various filter mediums for collecting PAH that are aerosols or have been adsorbed on dust particles; such information could aid in the design of personal worker "badges" to monitor particulate matter which could lodge inside the lungs.

According to current plans, Bill Parkinson will take a mobile unit to various coal-conversion pilot plants in such cities as Pittsburgh and Tacoma, Washington, to evaluate such instruments as a portable mass spectrometer and a portable infrared spectrometer as possible real-time monitors in a work environment.

Assessing Environmental Impact

Since planned coal-conversion demonstration facilities are to be constructed with the help of federal funds, the National Environmental Policy Act requires that environmental impact statements be written for such plants. The Environmental Impacts Section of ORNL's Energy Division now has a Fossil Energy Environmental Project, which will be assisting ERDA in drafting environmental assessments and legally required impact statements. The project, headed by Chuck Boston, also prepares environmental assessments on general coal-conversion technologies and on coal processes at specific sites. Next spring, if contracts are signed, a project team will be working with ERDA contractors in preparing environmental reports for coal-gasification plants to be built in southern Illinois and eastern Ohio. The proposed plants, which are to produce high-Btu gas that can be economically transported by pipeline, will be assessed to determine what their socioeconomic and environmental impacts will be. ORNL will later do assessments and statements for proposed low-Btu fuel gas plants and for fluidized-bed coal-combustion plants.

The project has been assessing the environmental problems posed by siting coal-conversion plants in three major coal-producing regions of the United States: Appalachia, the central states (such as Illinois and Ohio), and the West. Boston says factors that must be considered in siting these plants include the availability of water, quality and quantity of coal to be used, suitability of geology and climatic conditions, and socioeconomic considerations. In the case of high-Btu gas plants, there should be pipelines available to transport the product; in the case of low-Btu gas plants, there should be nearby industries that can utilize the fuel.

Project employees are compiling an environmental monitoring handbook for use by ERDA contractors in designing monitoring programs for coal-conversion plants so as to minimize discharges of hazardous materials that could threaten human health. Another effort under way in conjunction with the Environmental Sciences Division is the planning of an experimental landfill for solid wastes from coal-conversion plants. After the site for the landfill is selected, the staff will monitor surface water and groundwater to obtain baseline data before ash and slag from operating pilot plants are deposited. The groundwater will then be monitored to determine what materials are leached out of the landfill. One possible problem noted by Helen Braunstein in her information overview of landfills for coal-conversion wastes is the disposal of elemental sulfur, since one can expect a daily production of 100 tons of sulfur from a demonstration-size plant and of 1000 tons from a commercial-size, 25,000-ton-per-day plant using coal that contains 4% sulfur. Sulfur, if widely dispersed as a powder, can pose an environmental problem by rendering soil acidic enough to be infertile. Braunstein writes that alternatives to throwaway disposal being
considered include new uses of elemental sulfur for paving materials, plastics, and thermal and acoustical insulation.

**PAH in Perspective**

Like ionizing radiation, PAH are a part of man's natural environment as well as a by-product of modern industry. An excellent attempt to put the PAH problem in perspective has been made in the Information Division's document entitled "Environmental, Health, and Control Aspects of Coal Conversion," a 1500-page information overview edited by Braunstein, Emily Copenhaver, and Helen Pfuderer. In her summary of the document, Braunstein writes:

"PAH, some of which are potential health hazards, are thought to have been in man's environment throughout man's history. They are found in small but detectable concentrations in air and water as well as in soil samples of all types, including those distant from highways and industries. PAH in soil are thought to arise from natural sources such as pyrolytic decomposition of..."
wood, transformation of plant organic matter, and activity of soil microorganisms. Thus, although PAH may be produced and released by man’s activities, not all environmental concentrations can be assumed to have originated from anthropogenic sources; certain bacteria and plants synthesize PAH during normal development and thus provide a natural background level of PAH as high as 100 \mu g/kg in the upper layers of the earth. Estimates for total BaP emissions in the United States vary between 500 and 1300 tons annually. By far the greatest contribution is from both residential and industrial coal use for heating and power generation, although, surprisingly, forest fires account for more than 10% of the total.”

Braunstein notes the hazards of PAH: “Possibly the most health-endangering coal-derived compounds are PAH; many are known animal carcinogens and suspected human carcinogens. Workers exposed to high levels of PAH-containing coal volatiles show an increased incidence of skin and lung cancers. BaP, a component of coal tar and an identified carcinogen, is the most tested PAH and also the compound often chosen as the indicator compound for monitoring PAH... BaP has produced tumors in mice, rats, hamsters, guinea pigs, rabbits, ducks, and monkeys by oral, skin, and intratracheal administration.

“Humans are most likely to encounter PAH by accidental ingestion or skin contact. From laboratory-animal studies we know that many PAH ingested with food or water are largely eliminated in feces, indicating poor absorption from the gastrointestinal tract. Repeated application to the skin of mice, however, caused pathological changes in the blood, spleen, lymph nodes, and bone marrow, effects which suggest that PAH can be absorbed subcutaneously.”

The PAH problem is further complicated by the fact that mammalian enzymes responsible for PAH metabolism may either inactivate PAH or activate them to more carcinogenic forms. In addition, Braunstein states:

“Tumorigenic activity of PAH can be altered significantly by association with other materials... For example, PAH carcinogenesis is enhanced in animals by exposure to PAH in the presence of chemicals such as iron oxides and long-chain aliphatic hydrocarbons, or is inhibited by materials such as Vitamin A and selenium.”

Since man’s exposure to PAH is likely to increase in the age of the energy crunch, it is a hopeful sign that biomedical research may find ways of using natural compounds such as selenium and Vitamins A and E to suppress the activity of PAH carcinogens in man.
A Pitfall in Computation

When a person is solving a system of equations for some unknowns, it is not enough to choose a solution which makes the residuals small. This may be illustrated in the case of a pair of linear equations in two unknowns $x$ and $y$, suggested by C. B. Moler:

\begin{align*}
0.780x + 0.563y - 0.217 & = 0 \\
0.913x + 0.659y - 0.254 & = 0 .
\end{align*}

Suppose that an approximate solution to the system is given by $(x_1, y_1) = (0.999, -1.001)$. Then by substitution we note the residuals to be

\begin{align*}
0.780x_1 + 0.563y_1 - 0.217 & = -0.001343 \\
0.913x_1 + 0.659y_1 - 0.254 & = -0.001572 .
\end{align*}

Suppose another approximate solution to the system is given by $(x_2, y_2) = (0.341, -0.087)$. Then by substitution we note the residuals to be

\begin{align*}
0.780x_2 + 0.563y_2 - 0.217 & = -0.000001 \\
0.913x_2 + 0.659y_2 - 0.254 & = 0 .
\end{align*}

If one chooses a solution by the criterion of small residuals one chooses $(x_2, y_2)$. In fact the true solution can be obtained to be $(1, -1)$. And the approximate solution $(x_1, y_1)$ is closer to the solution $(1, -1)$ than $(x_2, y_2)$.

In order to answer the question, which solution is really better, one must decide on the criterion of goodness. It could be a small residual, or closeness to the real solution, or perhaps something else. And one will want different criteria for different problems. The pitfall to be avoided is the belief that if one criterion is satisfied, then all other criteria are necessarily satisfied.
Health physics, invented by K.Z. Morgan, is a many-splended discipline. For example, John Auxier, until last April director of the Health Physics Division, earned his first two degrees in physics, and his doctorate in nuclear engineering. He is a certified health physicist, but so are chemists, ecologists, radiation biologists, earth scientists, mathematicians, and veterinarians. Since the bombs first fell on Hiroshima and Nagasaki, study groups spanning this list have been mustered to bring some order and comprehension to those catastrophic events and their consequences. The longest lived and most productive of these was the famous ABCC, which stands for Atomic Bomb Casualty Commission. Since he joined ORNL in 1955, Auxier has been active in this group, making many trips to Japan and setting up innumerable prototype experiments in the Nevada desert. Here he recounts something of the historical background of the Commission, as well as some of the information it has gleaned that is useful to humanity's understanding of radiation exposure. ABCC has become Radiation Effects Research Foundation, to which, last year, Auxier was appointed consultant. This article is excerpted from a book to be published soon in the ERDA Prestige Series entitled "Ichiban: Radiation Dosimetry for the Survivors of the Bombings of Hiroshima and Nagasaki."

Hiroshima and Nagasaki
Thirty Years of Concern

By JOHN AUXIER

AUGUST 6, 1945, dawned hot and sultry in Tokyo. The Pacific War had been going very badly for Japan, and American bombers were wreaking havoc almost constantly in most parts of the Japanese islands. More than half of Tokyo was in ashes. At 8:16 AM, the Tokyo control operator of the Japan Broadcasting Corporation noticed that the Hiroshima station had gone off the air. He telephoned the station, but found the line dead; he could not get a call through to Hiroshima. About 20 minutes later, the Tokyo railway telegraph center realized that the main telegraph had stopped working just north of Hiroshima. From several railway stops within 10 miles north of the city, there came unofficial and confused reports of a terrible explosion in Hiroshima.
The end of World War II was brought about by the strategic detonations of two unprecedented bombs that also opened up a new technological era. Perceived as a turning point in scientific as well as military history, the event occasioned an inundation of reportage, exposition, and comment in the world’s communication media, a flood that did not begin to abate until several years later. The bomb was referred to as the Atomic Bomb, and nearly all that could be said about it appeared to have been said. Nonetheless, the fact remains that none of the salient details of those strikes—the yield of either of the bombs, positions of the release, wind and plane velocities—had been written into the Air Force records. That information was classified, and was largely kept in fragmentary form in the heads of the pilots and weaponeers. It was for the ORNL researchers, who came later, to deduce these parameters from residual evidence.

It goes without saying that of principal concern, then and to this day, is the impact of the holocaust on the populations of the two cities on which the bombs were dropped. Groups were formed almost immediately, in Japan and in the United States, to deal with the trauma and, ultimately, to assess its extent. This assessment required obtaining accurate figures for dose and medical effects and a correlation factor thereof. The following is a brief account of this 30-year study, in which Oak Ridge National Laboratory, through its researchers and technicians, played a key role.—Editor

The Japanese II Army Corps had its headquarters in Hiroshima, with a subsidiary Central Command Headquarters in Osaka, about halfway to Tokyo. About 9:00 AM, Osaka Headquarters reported to Tokyo General Headquarters that their communications with Hiroshima and points west had failed. Tokyo General Headquarters tried several times to raise the Hiroshima communications center, which was in an earth-and-concrete bunker next to the moat of an old castle, but there was no answer.

By the afternoon of that day, the Tokyo authorities had sufficient information to know that something very serious and different from an ordinary bombing had hit Hiroshima. There had been only three planes, and only one bomb had been dropped.

About 1:00 AM the next day, the radio monitors near Tokyo picked up broadcasts from the United States of President Truman’s announcement that the bomb was atomic and that Japan would be in total ruin if she did not surrender. President Truman said that the yield of each bomb was “equivalent to 20 thousand tons of TNT.” Although this was known by the designers to be a nominal figure given to the president for rhetorical purposes and to ensure minimal release of classified information, the actual yields had to be ascertained from information derived later from weapons tests and from scraps of data gleaned over subsequent years, largely in Japan. The vice-chief of the Army General Staff, Lt. Gen. Seizo Kawabe, was awakened at dawn on August 7 to receive a terrifying message from a high official in Hiroshima that “the whole city of Hiroshima was destroyed by a single bomb.” Kawabe was one of the few Japanese officials familiar with Japanese atomic research. He sent for Dr. Yoshio Nishina, a world-renowned physicist who was entirely familiar with nuclear fission and its possibilities and who had worked in Niels Bohr’s laboratory in Denmark before the war. Several years previously, in fact, Nishina had asked the army for a small sum to investigate the possibilities, but had been laughed at for wild-eyed dreaming.

A Japanese nuclear physicist, Dr. Sakae Shimizu of Kyoto University, performed detailed and knowledgeable studies in Hiroshima during the weeks immediately after the bombing. Unfortunately, soon after the war ended and while his studies were still under way, the U.S. occupation force confiscated the cyclotron and all apparatus and records that laymen would consider to be related to atomic-bomb research. Included in the latter were Dr. Shimizu’s instruments and notebooks. Through the handwritten receipt that had been given the professor, the confiscating officer was identified some 12 years later and eventually located in civilian life. However, soon after
Neutron and gamma-ray dose as a function of distance from ground zero in Hiroshima and Nagasaki.

receiving the materials from Dr. Shimizu, the officer had been ordered back to the United States with little time for an orderly changeover, and subsequently everything was lost.

Nishina left for Hiroshima as soon as possible, but did not arrive until the afternoon of August 8. In only a matter of hours, he had found convincing evidence of the nuclear nature of the bomb and, from the amount of radioactivity, estimated that it was equivalent to thousands of tons of high explosives. Nonetheless, it was not until August 10, the day after Nagasaki was hit by the second nuclear bomb, that the investigating committee was willing to accept Nishina’s conclusion that the Hiroshima bomb had been, in fact, a nuclear (or “atomic,” as it was then called) explosion.

As a result of the extent of human injury and suffering and the relative novelty of the large doses of radiation, several Japanese committees were set up to study the effects of such weapons. The cessation of air raids with the end of the war on August 14 made the study easier. All the observations made during August of immediate physical damage and medical effects were made by the Japanese. The work was thoroughly and carefully done despite the extremely difficult conditions in the cities.

Although most of the doctors and nurses in both cities had been killed and most of the hospitals destroyed or badly damaged, efforts were made to keep records on the injured who reached the remaining hospitals, as well as on the subsequent deaths. These records were invaluable when the investigating teams arrived later.

The Investigators Arrive

By September 1, at least four groups were on their way to Japan to investigate the bombings. In addition, a large subcommittee was organized by the Japanese Imperial Government, consisting of 90 physicians and senior medical students. Ultimately, all the groups were ordered by General MacArthur to unite to form the Joint Commission for the Investigation of the Effects of the Atomic Bomb in Japan. The cooperation among the medical sections of these groups was apparently excellent, and combined teams of Japanese and Americans studied thousands of survivors.

The groups working on physical damage, however, apparently did not cooperate as well with each other. For example, each group found that to correlate effects with distance from the epicenter, they had to determine the surface coordinates and height of this point. Each group seems to have made its own measurements and calculations to find the epicenter and apparently did not attempt to reconcile the different results to choose the most likely location in each city. At that time, the shadows burned by the fireballs were fresh and clear, and the measurements could easily have been reconciled. Twenty years later, it proved very difficult to choose the most likely locations.

In November 1946, an American team that included Paul Henshaw of Clinton Laboratories went to Japan. It chose the name “Atomic Bomb Casualty Commission (ABCC),” the name later chosen for the major, long-term program set up by President Truman through the National Research Council of the National Academy of Sciences. [In 1975, the ABCC became a jointly funded United States–Japanese operation and was renamed the “Radiation Effects Research Foundation (RERF).”]

In the earliest studies, it became apparent that if the work were to be accomplished, the radiation doses to the survivors would have to be known, but the technology for obtaining them did not then exist.

By 1952, Sam Hurst, Rufe Ritchie, and coworkers in ORNL’s Health Physics Division had developed several sophisticated dosimetry systems, and the AEC asked them to commence studies of the radiation fields, using the nuclear weapons tests then being conducted in the Nevada
From these tests, in 1953, the instruments were proven successful; by 1955, a refined dosimetry system was ready for the ORNL health physicists to use in tackling the dosimetry problems of Hiroshima and Nagasaki. Hurst and Ritchie played a major part in setting up the program and in supervising the field operations through 1957. In determining the exact dose delivered to the Japanese victims, studies of the energy and angular distributions of neutrons and gamma rays from weapons were made; the shielding characteristics of building materials and Japanese houses were measured; and the effect of the air-ground interface on the radiation fields as well as numerous other parameters were quantified.

These experiments were terminated in 1958 with the cessation of above-ground weapons testing. Still to be determined, however, were the correlations of dose to distance from source, through air. Field experiments in 1962 and 1965 used the 1527-ft BREN Tower, on which hung a large cobalt-60 source, the Health Physics Research Reactor, and a neutron generator capable of providing the world's most intense stream of 14-MeV neutrons ($10^{13}$ neutrons/sec).

By 1965, the “air dose” curves had been developed, as well as simple but accurate equations to describe the shielding provided by houses. These data were designated T65D, for values as of 1965, but tentative (T), pending removal of several uncertainties. The uncertainties have now been narrowed to about 15%. Also since 1965, computer programs and techniques have been developed for estimating the doses to organs of the body, including fetuses, of which more will be said later. Calculations of doses to persons who were exposed inside typical Japanese dwellings and commercial buildings were completed years ago. Recently, estimates have been made for other structures, especially large buildings of reinforced concrete.

**Ichiban**

In all, some 2000 scientific, technical, and supporting investigators, at a cost of about $200 million, have been working for over 30 years to assess medical effects and the amount of radiation, and then to correlate the two statistically, to determine the dose received in Hiroshima and Nagasaki in 1945. Why this huge expenditure of money and time? The program of determining and supplying individual dose values to the population under study by the ABCC was termed in Japan the Ichiban (meaning No. 1, the first, the greatest) project because of its importance. Simply stated, to predict the effects of radiation on humans, we had to be able to correlate the dose and effects as they pertained to the affected Japanese.

The approach was to obtain as much quantitative data on animals of various species for many types of radiation in the hope that extrapolation to humans would be possible. These extrapolations should then be verifiable by actual data on humans.
for such exposures as were known. For this verification, the largest and most important group of normal, healthy humans ever to be exposed to high levels of radiation was the surviving population of Hiroshima and Nagasaki. Further, the two bombs produced significantly different types of radiation fields. However, at the time this purpose for obtaining the doses was established, there was no great intrascience debate about the effects of low levels of radiation as there is now. More than ever, the fate of all radiation-related activities is subject to public concern and governmental regulation. The data from Japan cannot settle the debate—which may at this point be beyond the realm of science—but they may well provide answers to some critical questions concerning the "linear-vs-threshold" theories; these data are limited, of course, to acute exposures.

What types of radiation effects have been observed in Japan that may be related quantitatively to dose? As mentioned earlier, radiation-induced cataracts were observed. However, for this particular effect, the number of cases and the different conclusions and descriptions furnished by ophthalmologists make the task impossible; suffice it to say that for whole-body exposures of gamma rays, the probability of other effects is much higher. For other types of radiation and exposure primarily to the face, the risk could be increased, as it was in the case of the early cyclotron workers whose eyes were exposed to the beams. One of the most marked effects, in terms of percentage, was that of microcephaly—small head size—observed in children who were exposed as fetuses during the first three months of pregnancy. This condition was frequently accompanied by some mental retardation as well as generally smaller stature. Although there were relatively few pregnant women exposed to high levels of radiation during the first trimester, the incidence of microcephaly in the child so exposed was the highest of any observed effect.

The most serious and most publicized effect, in terms of the number of persons affected, is leukemia. Although some increased incidence of leukemia was observed within years and the incidence rate remains somewhat above normal today, the period of 1953 to 1956 (8 to 11 years after exposure) was by far the worst. The 30-year probability of leukemia from these exposures ranged from about zero for doses of less than 50 rads to almost 1% for persons exposed at 400 rads. There has been some concern that other forms of cancer might also be increased by the radiation, and there appear to be some increased tumors, both benign and malignant, in the most highly exposed groups. However, even though the exposures occurred years ago, the data are not conclusive.

No Genetic Effects Observed

What about genetic effects? In the first report of the ABCC, made in January 1947, a section of considerable length was written by Lt. James V. Neel on plans for a program to seek genetic effects of the radiation. He recognized that even a midlethal dose of radiation (then considered to be about 500 roentgens) would produce only small genetic effects, and that most persons who had received this amount probably died from the combined effects of radiation plus blast, flash and flame burns, flying debris, etc. Dr. Neel, who has followed the genetic studies since 1946, is now a consultant to ORNL. No genetic effects have been observed in the survivors or their offspring. There are now numerous survivors whose children were conceived after the bombings and who have subsequently become grandparents.
In summary, there were indeed statistically significant radiation effects on the persons who survived the initial trauma of the bombings. Can any of these effects be related quantitatively to the doses that caused them? Yes, there is good correlation between the doses received by a fetus during the first trimester of pregnancy and the probability of the child developed from that fetus having microcephaly. The same can be said for bone marrow dose and leukemia. Other effects may be found to be relatable as the study of organ doses progresses.

Many at ORNL have contributed to these studies. As indicated earlier, Sam Hurst and Rufe Ritchie played most important roles in the early days and have continued to help from time to time. K. Z. Morgan gave strong encouragement. I am the only one of the original Ichiban group still involved; until his retirement, Joe Cheka was always in the program. Experimental research is being performed today by Troyce Jones and George Kerr. I have attached a list of Oak Ridge names, all of whom contributed at some time or other, sometimes as key scientists, sometimes as a pair of willing hands in the Nevada desert. We all believe it was worth the effort; in the process of fulfilling our mission, we have provided more fundamental data and understanding of the radiation fields from nuclear weapons (as well as other intense radiation sources) than any other group of scientists.

The following scientists, engineers, and technicians from ORNL have contributed their service and talents to the Ichiban project:

<table>
<thead>
<tr>
<th>E. T. Arakawa</th>
<th>P. N. Hensley</th>
<th>P. W. Reinhardt</th>
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<tr>
<td>J. A. Auxier</td>
<td>H. H. Hubbell</td>
<td>R. H. Ritchie</td>
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<td>T. V. Blosser</td>
<td>G. S. Hurst</td>
<td>F. W. Sanders</td>
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<td>J. S. Cheka</td>
<td>T. D. Jones</td>
<td>C. Sartain</td>
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<td>F. J. Davis</td>
<td>G. D. Kerr</td>
<td>W. H. Shinpaugh</td>
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<td>J. A. Harter</td>
<td>K. Z. Morgan</td>
<td>W. S. Snyder</td>
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<td>F. F. Haywood</td>
<td>P. T. Perdue</td>
<td>J. H. Thorngate</td>
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Of those Hiroshima children exposed in utero before the 18th week of gestation, these percentages were born with small head circumference, relative to the radiation dose.

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**Staff Quote:**

"During my stay at Orsay, France, I found a great interest in our new heavy ion venture at Oak Ridge. Perhaps this was stimulated from concentration on their own heavy ion venture with GANIL. I was asked numerous questions about design characteristics of our machine and, in particular, about our philosophy for a computer system to handle both the data taking and data analysis at Oak Ridge. At the seminar I presented on the status of our heavy ion project, there was a continuation of these numerous questions and comments. Needless to say, there was great curiosity as to what are our chances for the realization of our Phase II plans which would allow us to achieve energies in the range of 100 MeV-nucleon and thus have a system comparable to their GANIL."—Noah Johnson, discussing his February 1977 stay at the University of Paris, South, in Orsay, France.

WHAT SOCIAL AND POLITICAL mechanisms weave scientific and technical discoveries into our economic fabric? Dr. Dawson has chosen the development of nuclear power as his case history for examination of that question. The result probably will remain the best documented study of the political history of that development.

Those of us who were part of the technical development of nuclear power may find fault with some of Dr. Dawson’s choices of emphasis and may object to what, to us, are significant omissions. In some instances, those objections are justified, but I decided while reading the book that in the past I often had been too close to my individual trees to see the forest: Technological demonstration is not nearly enough for economic and social acceptance, and the process of acceptance is much more complicated and precarious than our intuition predicts.

Our institutions—in this case Congress, its Joint Committee on Atomic Energy (and individual members of those bodies), the public utilities, manufacturers, the President, the courts, the labor unions, the state governments, the banks, the defense department—and uninstitutionalized forces—a public dream of Utopia, a fear of radioactivity, and a terror of nuclear weapons in the hands of other nations, possibly of undefined, and hence unpredictable people, or even of our Air Force, Navy, and Army—have had and are having as much influence on the acceptance of nuclear power into our culture as the required technological development.

This book is largely concerned with the institutional aspects of that acceptance. It will be useful to those who wonder why it has taken a sesquigeneration to move from Hiroshima to our present, somewhat clouded, peaceful exploitation of nuclear energy and to those who wonder why nuclear energy has been allowed to become an important source of our energy supply.

In his study of the development of nuclear power, Dr. Dawson uses the concept of “technology delivery system,” for which he credits Dr. Edward Wenk, Jr. A discussion of that concept and the model used by Dr. Dawson appear in the last chapter, and a diagram of the model appears on page 225. In the model, the results of basic knowledge and basic and applied research are combined with the “physical environment”—capital, specialized manpower, tools, and natural resources and energy—by private and public “management” to overcome “impediments” and produce the “desired outputs” and “undesired outputs.” Management is strongly influenced by local, state, and federal governments through regulation, sponsorship, and direct participation. Those governmental activities, in turn, result from the influences of special interests, public interests, and the social environment or “body politic.” The impediments include “conflicting social value preferences, inadequate information and its flow, bureaucratic inertia, etc., and may occur anywhere in the delivery system.”

Economic competition from other existing or prospective systems with similar products does not appear explicitly in the model, but perhaps it is included in “conflicting social value preferences.” The chapter then continues with the evaluation of the performance of the technological delivery system that resulted in competitive nuclear power.

After his introductory first chapter, Dr. Dawson uses the next four to outline, more or less chronologically, the pertinent technical and political history and, in Chapter VI, he gives a separate history of the “Regulation of Nuclear Power.” These histories are presented with a choice of
emphasis that leads to the discussion and evaluation in the concluding chapter.

Perhaps it is inevitable that information provided to fill the spaces in a two-dimensional diagram will, in aggregate, appear two-dimensional as well. Dr. Dawson writes in a clear, succinct, and readable style, and his discussions of conflicts among the Joint Committee, Congress, and the AEC are well documented, but personalities remain largely obscured. Nowhere in the book do we feel Walter Zinn's practical energy, Alvin Weinberg's scholarly enthusiasm, or Hyman Rickover's intolerance of incompetence. (On the other hand, we are given an inkling of James Ramey's aggressiveness.)

The technological history is amply complete for the purposes of Dr. Dawson's approach to his study. No doubt the technical knowledge displayed in the book derives from the fact that Dr. Dawson, during his years at Hanford, was an active contributor to reactor development. Perhaps it is to avoid showing partiality that he names very few actual technical contributors to nuclear power. (An exception is ORNL's Herb Pomerance, whom he credits with discovering hafnium as the principal neutron absorber in commercial zirconium. This discovery led the way to the development of Zircaloy—spelled "zircalloy" in the book—the cladding material for the fuel in most light-water reactors.)

But here again, I frequently found myself wishing that the study had been fleshed out to include more of the personalities of key individuals. A history or study of a human process cannot be complete without that third dimension to account more fully for the force behind certain proposals and for specific key decisions.

One curious omission is that of the Advisory Committee on Reactor Safeguards and its first chairman, C. Rogers McCullough. As I recall, many of the concepts now applied by the nuclear regulatory bodies were developed by the ACRS during its early years.

The book contains a few errors in fact. For example, Dr. Dawson on page 89 erroneously states that the blanket of the Aqueous Homogeneous Test (HRE-2) contained thorium. Generally, however, the technical history is as accurate as one would expect from a well-informed person who had actually been involved in that development.

Most of the work on this book was done in 1971, and at that time, nuclear power seemed well accepted by the general public. Since that time, that acceptance has been partially reversed. The recent change in the attitude of at least some of the public does not invalidate the impartial analysis presented in the last chapter. Rather, it represents a new phase in the history of nuclear power, a study of which could begin where Dr. Dawson's has ended.

I recommend this excellently documented book: as a source of information on the history of the development of nuclear power, as a nostalgic and educational trip for those who lived part of that history, and as a study of the development and management of a technology.

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Staff Quote:

"My trip to examine waste heat utilization by Électricité de France was very valuable for identifying new technologies for using waste heat as an alternative energy source for agriculture and aquaculture. France is clearly ahead of most U.S. research efforts in this field and is making definite plans for dual-purpose power plants. I feel that the United States has mistakenly given waste heat utilization a low priority by assigning it to the realms of (1) "cosmetic" efforts to counter thermal pollution problems, and (2) solely an energy conservation role, rather than recognizing its value (as the French have done) as an alternative energy supply technology with near-term applications."—Chuck Coulant, commenting on his visit to France to tour facilities making beneficial use of power plant waste heat for raising fish and vegetables.

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Several years ago, Jeff Tester wrote an article for the Review describing the impact of the Massachusetts Institute of Technology Practice School on the Laboratory. In this article, Bill Ayres, director of the school for the past year, explains the skyrocketing growth in chemical engineering enrollment in terms of its beginnings in the last century, and its development during its brief history. Bill came to ORNL in January 1976 as assistant director of the school, following a semester as assistant director at the Bound Brook, New Jersey, location. Prior to that, he had received his M.S. and Chem. E. degrees at MIT. (Since leaving ORNL, Tester has co-authored a book with Stan Milora, now in the Fusion Energy Division, entitled Geothermal Energy as a Source of Electric Power, MIT Press.)

Today's MIT Chemical Engineers

By WILLIAM AYRES

THE EVOLUTION OF chemical engineering can be traced through the development of its method of analysis. From a foundation in mechanical engineering, chemistry, and applied physics, its practitioners developed new methodologies through the examination of problems common to large-scale reaction containment, control, and product separation. The organization of similar chemical process operations through the concept of unit operations—with its analysis of heat, mass, and momentum transfer and the development of empirical correlations—prepared the way for a generalized approach to the underlying transport phenomena based on the physics of continuum mechanics. Advances in the determination of thermodynamic properties, modeling of complex reaction systems, and computer simulation of process dynamics have further generalized the perspective of chemical engineering and have resulted in a continued decrease in the heuristic content of the discipline. Since the Practice School was established at the Massa-
chusetts Institute of Technology in 1917, the ratio of descriptive to quantitative material in the curriculum has greatly decreased, but the necessity of developing judgment in the application of the available methods has not.

Of the three graduate chemical engineering degrees awarded at MIT, both the master's degree in chemical engineering practice and the chemical engineer's degree require a semester at Practice School. Since 1948, with the four-year exception of 1962–1966, the students have spent half that semester at the Oak Ridge site and often make their first substantial contributions to chemical engineering here as part of the research and development activities of ORNL.

How MIT School Works

Project suggestions for the students are now solicited twice a year from the ORNL staff, and from such suggestions those projects that are appropriate in their education content and which contain objectives that can be achieved within a one-month period are chosen. Three or four students are assigned to each project, and one of them is designated group leader. A problem statement, with references to the literature, provides a basis for analysis. The initial assessment and experimental plan are formally presented in an investigation memo and at a proposal conference, where the ORNL staff members who suggested the problem and MIT staff review the proposed activities.

Development of effective oral presentation skills is an important component of the program. In addition to the proposal conference, two progress reports and a final oral presentation provide ample opportunity for the students to devise visual aids and structure their presentations to deliver a concise message with a style that leaves room for their personalities. Each presentation is tape-recorded for the student and, in
Heavy work goes on in the school's library in preparation for the oral presentation. In addition to their reports, the students prepare their own slides (see clothesline in background).

preparation for the final presentation, a rehearsal is videotaped. A good deal of denial—"That's not me"—usually occurs when the student watches the replay.

Each group also provides a written report on its work. These reports, usually 30 to 40 pages in length and in formal thesis format, have consistently adhered to a tradition of high quality. Many have been published in engineering journals, and requests for past reports from within ORNL are frequent.

The wide applicability of the methods of chemical engineering enables the students to work on projects in a variety of disciplines. Regardless of its origin, a project's central issue can usually be classified as a problem in transport phenomena, kinetics, or chemical thermodynamics. Most of the problems involve transport phenomena—either the design of a transport system, such as a heat exchanger, or the experimental determination of a transport parameter, such as a mass-transfer coefficient.

Transport Phenomena Studies

Several groups have worked with J. S. Watson, C. W. Hancher, and J. M. Begovich to determine dispersion and mass-transfer coefficients in both tapered and cylindrical three-phase fluidized beds that are suitable for coal-liquefaction and microbiological processes. However, the hydrodynamic and interphase mass-transfer characteristics are not completely understood. For the coal-liquefaction and gasification application, two other groups have worked with H. D. Cochran, P. R. Westmoreland, and R. E. Barker to mathematically model the hydrodynamics—specifically the recirculation rate—in a modified bed design.

Packed-bed adsorption of krypton gas from LMFBR and HTGR reactors has been studied with a carbon dioxide-water model system to simulate krypton adsorption in liquid carbon dioxide. Most recently, Enoch Chao, Bob Bertolami, Jean Varlet, and Gary Wilkes, with assistance from A. D. Ryon, J. M. Begovich, and T. M. Gilliam, examined the column operation and mass transfer for several types of packing.

In the Chemistry Division, a computer simulation and experimental verification of composition-dependent coefficients for ion transport in molten cells were carried out by Georges Duret, Bob Hossan, and Mike Rill under the guidance of Jerry Braunstein.

The interaction of coal-derived carcinogens with the environment and its inhabitants is also an area in which the students have employed their knowledge of transport phenomena and applied mathematics. Working with Steve Herbes of the Environmental Sciences Division, Bernard Tao, Dan Dershowitz, and Ralph Troiano approximated the uptake of aromatic hydrocarbons by aquatic microorganisms with a model system of suspended yeast cells. The distribution coefficients of the labeled hydrocarbons were determined and compared in terms of molecular properties and possible surface interaction models.

To examine the effects of chronic exposure to suspected carcinogens, B. C. Pal of the Biology Division has been developing a controlled-release implant. Fola Awokoya, Steve DeCicco, Jay Dweck, and group leader Pam Whitman developed an equation for the in-vitro diffusion of a carcinogen through the composite implant and compared the solution with their experimental release rate data. Their mathematical model now simplifies estimation of the in-vivo carcinogen dose.
Designing Transport Systems

Projects that require the design or assessment of transport systems (heat and mass transfer, separation processes) are the second most frequent. Heat-transfer problems such as the determination of temperature profiles in a prototype HTGR fuel rod, calculation of heat losses from the ACES system, and the design of heat exchangers to supply liquid helium to test magnets for the fusion program have allowed students to develop judgment in assessing complex problems and to gain experience in analyzing their assumptions through computer simulation. Pam Whitman and Jan Pinkowish recently worked toward a finite-differences solution of transient, three-dimensional heat transfer during multipass welding of a thick metal slab, and Jim Lee, Karen Kraftick, and Jay Dweck devised a mathematical model to calculate the temperature profile and tritium mass-transfer rate in a new lithium blanket design.

Transport problems in solar-powered processes have included the design of a solar evaporator for the dehumidifying section of an air conditioning system and the design of ammonia evaporators for the Ocean Thermal Energy Conversion system. This system uses the solar-heated water of the ocean surface to vaporize ammonia for turbine-generators and condenses the ammonia with cold water pumped from about 1500 ft below the surface.

Systems in which the conditions of transport are not completely understood require experimentation to develop correlations between a measure of performance and operating variables. Fola Awokoya and Steve DeCicco pursued one such project with Josh Johnson. Their goal was to determine the feasibility of separating waste oil from oil-water emulsions with a crossflow,
Jim Lee, Karen Kraftick, and Jay Dukeck work on a heat and mass-transfer problem for a fusion device lithium blanket design. Jay, incidentally, has distinguished himself by earning his B.S., M.S., and Chem. E. degrees in chemical engineering, and a B.S. in mathematics, all in four years. During one term, he was taking 12 courses and playing violin in the MIT orchestra.

Dynamic-membrane, hyperfiltration unit. The degree of separation was correlated with operating pressure across the membrane and the circulation velocity of the effluent. Steve decided to stay in Oak Ridge and is now working with the Chemical Technology Division.

Similar projects have included the drying of ion-exchange microspheres in a fluidized-bed, hydroclone separation of micrometer-size solids from coal-liquefaction product streams, and foam fractionation of surface-active biomolecules. The latter is part of an ongoing effort with G. P. Hirsch of the Biology Division to develop new separation techniques for the initial isolation of cellular components from tissue.

Occasionally, we receive a request to perform preliminary design calculations for an industrial separation process. Brad Johnson, Wei Choi, John D’Acierno, and Paul Stiros designed a multistage extraction process for recovery of the zinc chloride catalyst in the University of Utah’s coal hydrogenation process. Their cost analysis of the recovery step showed it to be the controlling factor in the economic viability of this coal-conversion process.

Chemical Kinetics Studies

Problems in chemical kinetics, although infrequent, are greatly appreciated. Kurt Kraus and Fred Nelson were consultants for an investigation of hypochlorite interaction with activated carbon. This problem arose from a side reaction in an oxidation-filtration system to remove silver from photograph-development waste streams. The supposedly treated and purified effluent had a brown color which was thought to arise from a reaction between hypochlorite and the activated carbon filter. James Mbu, Dan Dershowitz, and Jose Monge investigated the apparent reaction between the two and made preliminary attempts to identify the source of the color. The kinetics of microbial systems is becoming a chemical engineering specialty. Two groups studied the population kinetics and nitrate utilization rate of the denitrifying bacteria Pseudomonas stutzeri in batch and flow reactors. Under anaerobic conditions, the microorganism can reduce nitrate wastes from uranium processing to nitrogen, thereby decreasing the nitrate level in effluent streams.

This review of some of the 62 projects completed during the last three years indicates the range of problems with which Practice School students work. The generality of the methods of chemical engineering, originally developed for the solution of industrial problems, is perhaps best highlighted by their applicability to the problems of such descriptive fields as biology. Indeed, the need in biology and medicine for unifying concepts and for effective analytical methods to simulate physicochemical dynamic interactions is reminiscent of the early stages of chemical engineering. This versatility of the discipline explains, in part, its growing appeal to undergraduates interested in a career in engineering, medicine, or technical management.
LEUKEMIA IS A CANCER of the blood-producing cells in the bone marrow which causes an overproduction of the white blood cells called leukocytes. The customary treatment of leukemia is the introduction of ionizing radiation or drugs to kill the cancerous cells, but this treatment halts the bone marrow’s activity and thus the manufacture of granulocytes. Without granulocytes—the white blood cells making up the body’s infection-fighting forces—the patient becomes vulnerable to certain bacteria and fungi.

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The result is that an overwhelming majority of leukemia patients die of infection, even when the cancer itself may be under control.

To combat this vulnerability, medical doctors try to supply the afflicted patient with the disease-fighting white blood cells in quantities sufficient to restore natural resistance. Work on this treatment is being done in many clinics, with machines that remove whole blood from donors, centrifuge it to separate the granulocytes for transfusion into the leukemic patient, and return the depleted blood...
Bud Breillatt was hired by Norman Anderson in 1967, first as a postdoctoral, then as a group leader of the centrifugal systems group in the MAN Program. When Norm left, Breillatt became acting director of the MAN Program, which has since become part of the Biology Division. In 1972, Breillatt's interest in blood-cell separation became dominant, and from this preoccupation evolved CYTRIAGE, an automated, centrifugal leukapheresis system for harvesting functioning granulocytes from living blood for replacement in leukocytopenic patients. The following account tells the story of this remarkable machine's development, and illustrates Breillatt's method of operation, which, he says, "...has been to lay a firm theoretical base on which to build a successful prototype program...by gathering together individuals who have expertise in the various required disciplines and are motivated by their interest in the project. I have become a multidisciplinary translator as a means of embodying my ideas in technical systems far beyond my own abilities to create."

to the donor, all in a continuous flow. The technology was developed in a joint project of the National Cancer Institute (NCI) and the International Business Machines (IBM) Corporation, over the period of 1964-1967. The machine so developed is capable of yielding enough white blood cells (5 to 15 billion) per daily 4-hr donation to provide temporary respite from infectious episodes. To free the patient from infection entirely, as many as ten times the number of functional granulocytes as these machines can produce must be administered daily. The machines now in use collect about 5 to 20% of the white blood cells available in the whole blood passing through the centrifuge; collection of 60% or more would provide sufficient cells to reverse the course of an infection.

This method of leukapheresis, or blood separation, centrifuges the whole blood so that it flows selectively to streams which are predominantly red cells, white cells, and plasma. It has delivered a low percentage of the white cells available, largely because the sedimentation of the red cells is hampered by the shear to which the rotors subject the blood. Another problem is that control of the flow has required determination of the location of the interface between streams by manual and visual means, which seriously limits the efficiency of the yield. And, finally, blood varies widely among donors.

Biochemist Julian Breillatt, veteran of the MAN Program's development of the zonal centrifuge, was worrying this problem like a dog with a bone in 1970 when he attended the annual meeting of the Federation of Societies for Experimental Biology and Medicine in Atlantic City. There, in informal discussions of the problem, the only response he could elicit was, "That's a good problem, a real dandy. Wouldn't touch it with a ten-foot pole."

His concern intensified later that year, while he was on leave at the University of Utah where he had done his graduate work. It was there that he was made aware of the terminal illness of a cousin, LeRoy Stevens, president of the Association of Business Colleges and head of Stevens-Henegar Business College in Salt Lake City. He was a victim of sarcoma.

Discussions with his cousin's doctor, George E. Cartwright, gave Breillatt a new impetus to try to improve the efficiency of the blood-separating centrifuge, and he returned to Oak Ridge with this specific goal. One of the problems, he had been persuaded, was how to enhance rouleaux formation. Red cells sediment in the form of worm-shaped stacks—so-called rouleaux—that have great instability and shatter easily. Affecting them is the shear of fluid flow, in which layers of a fluid move past a stationary surface at different rates which increase with their distance from the surface. Also, turbulence is a problem. A redesign of the rotor to minimize shear and turbulence seemed to be in order.

The New Concept

Back at the MAN Program laboratories, Breillatt pondered the problem. For a year, he scrutinized a film made by IBM, read the
This cross section shows the Cytriage mechanism. Instead of the shallow, broad, rounded bowl of the original centrifuge, the Cytriage has three distinct stages in its stream. The first is the reformation chamber, in which the rouleaux, disturbed from the turbulence of the feed port, are given a chance to reform. The second is the radial flow chamber, in which the red blood cells are taken off, leaving the plasma and white blood cells. The third stage is the axial flow chamber, at the end of which the plasma is selectively returned to the center of the spinning container, leaving the white blood cells to be drawn off in high concentration.

In May 1972, Sartory conceived a design, emerging from his theoretical model of blood cell sedimentation, which ultimately became the answer. With that as a start, the three innovators, by now adapted bioengineers to a man, proceeded to work out the details for prototypes of two new, vastly improved blood centrifuges. Eventually, the two evolved into a three-stage separator of novel design.

Where the NCI-IBM rotor was primarily an axial flow system, the new design had the separation chamber elongated in a radial direction but short axially. Feed blood was injected into an annular zone and held by centrifugal force between the denser packed red cell phase below and the less dense plasma above. The separation process consisted of the sedimentation of red-cell rouleaux to the periphery of the zone, with the leukocytes and plasma flowing centripetally through the zone and out the top. The separation chamber allowed appreciable rouleaux formation because it offered low shear stress. In the old rotors, the rouleaux had to be formed before they entered the separation channel. The determination and control of the interface of plasma and red blood cells were yet to be invented, but the problems involving the physical properties of the blood seemed to be conquered.
Dick Willis tinkers with the “brains in a drawer,” the highly sophisticated automated control system developed by him and Colin West.

Walt Sartory, L, and John Eveleigh confer on the merits of one of the components of the new centrifuge.

Ready to start its construction, the developers took their design to NCI. Although a measure of indifference greeted them at first, through the interest and support of their friend Jim Liverman (at the time in the process of moving from ORNL to the AEC administrative staff in Washington), they were eventually funded by NCI in 1973 to build their apparatus.

Monitoring and Control

Colin West was at ORNL at the time on an exchange program with Harwell. He and Dick Willis, of the program’s regular staff, designed and built the initial automated control system for the new machine. According to Breillatt, it is a system that today, although expanded in function, still employs the original basic concepts.

It is the accurate monitoring and control of the interface of the plasma and red blood cells that determine the efficiency of the white blood cell yield. Lou Thacker of the Instrumentation and Controls Division suggested the fiber optics that made detection and control of this interface possible. The contribution of John Eveleigh, member of the MAN Program staff, was his observation that the rotor’s plasma stream could furnish the necessary background value for the differential conductivity measurement and control of the composition of the feed blood.

Improvements continued to be worked in. The efficiency of the centrifuge was measured by a Cytofluorograf, a refinement of a Los Alamos development that is able to determine the percentage of granulocytes in each stream, identifying them by their individual fluorescing characteristics. Ron McKeighen, a nuclear engineer from the University of Illinois, working part-time with P. R. Bell and funded at ORNL by the Department of Commerce as a Presidential Scholar, joined the group, having learned enough computer programming from P. R. to adapt the
Professor Carl Remenyik stands beside a montage photo of a flow of blood undergoing a "hydraulic jump," a phenomenon which he discovered to be one of the events in the centrifuge that was preventing the red blood cells from sedimenting. In the inset is a photomicrograph of the red blood cells precariously stacked into rouleaux.

Jerry Brantley tunes the Cytofluorograp, an instrument that can give an accurate relative analysis of the amount of granulocytes in each stream, based on their fluorescing characteristics. Brantley has been responsible for the assembly and smooth running of the centrifuge from the first.

Cytofluorograp-PDP-8 interface and provide automated differential counts of the collected white cells.

Four patents were awarded for this achievement. The result is a silent, efficient centrifuge that is today extending lives. Its ability to recover from 70 to 100% of the white blood cells present in the feed blood has been demonstrated. Six prototypes are now under construction at ORGDP in the building that housed the MAN Program and at Y-12 in the Biology Division's machine shop, supervised by Sam Simmons and executed by Max Whitley. These prototypes will be given to NCI to distribute for experimental work in six qualifying cancer centers in the United States and abroad, the clinics to be determined on the bases of merit, qualifications of operating personnel, and their ability to contribute.

Anyone whose disease deprives him of a functioning bone marrow requires this leukocyte replenishment daily. After determination of the human lymphocyte antigen match between donor and recipient, the donor submits to a period of leukapheresis in which the machine takes whole blood, extracts nearly all the white blood cells into a storage bag, and returns the red cells and plasma to the system, all in continuous flow. At no time in this process is more than a half a liter of blood outside the donor's body. A healthy bone marrow will manufacture white blood cells immediately and continuously to make up the deficit. Shortly afterward, the collected white blood cells are injected into the granulocytopenic patient.

There is no risk to the donor, provided the rotor is kept scrupulously clean and sterilized—a detail which poses a problem. At present, the machine is made of materials that can withstand the abrasion and high temperatures that go with such cleaning, requiring that it be easily dismantled and assembled. A proposed improvement is to devise a disposable rotor to save on the labor cost of cleaning it.
IR-100 Candidate

The new centrifuge, now dubbed the Cytriage, has been entered in the Industrial Research IR-100 competition. In its present stage of development, it is a three-stage separator whose operating conditions are under automated control. The first stage is a chamber located along the axis of the rotor which provides a low shear flow regime in which red-blood-cell rouleaux can re-form after passage through the seal. The blood then flows to the radial-flow chamber, where leukocyte-rich plasma is separated from the red cells. This white blood cell and plasma phase then flows up an axial-flow separation channel, allowing the leukocytes to sediment away from the bulk of the plasma. The leukocyte concentrate is then drawn off as a product stream, and the red cell and plasma streams are combined and returned to the donor.

The speediness of any procedure dealing with a substance like blood is an obvious advantage. In clinical trials at NCI, performed by Drs. Robert Graw, Albert Deisseroth, and Richard Ungerleiter, granulocyte collection with the Cytriage has been achieved on an average of four times as fast as that obtained from the identical donors using the NCI-IBM systems. This collection rate is limited by the rate at which blood can be withdrawn from the vein and is expected to double at institutions where vein collapse on phlebotomy needles is avoided by placing arteriovenous shunts in regular donors.

Refinements to the current prototype system will include a sealless drive mechanism and replacement of the analog control electronics by a microprocessor circuit. Such improvements may possibly increase the granulocyte yield to some degree, but primarily they will contribute to a more simplified operation.

This work is described in several technical memos now on file at ORNL; the first, however, numbered ORNL/TM-3901, published right after Remenyik's and Sartory's double breakthrough in 1972, has a brief message on p. iii:

This work is dedicated to
LeRoy Robinson Stevens
and to his physician
George E. Cartwright

Awards and Appointments

At its meeting in February, the American Association for the Advancement of Science elected the following members of the ORNL staff as fellows: Loucas G. Christophorou, Charles F. Baes, Jr., Carlos E. L. Bamberger, and David G. Gosslee.

Now at ORNL from the Chemicals and Plastics Division of Union Carbide Corporation's South Charleston plant is the incoming director of the Instrumentation and Controls Division, Herbert N. Hill. He assumed that responsibility May 1, replacing retiring Director Cas Borkowski.

Recipient of the 1977 Herty Medal, awarded by the Georgia section of the American Chemical Society for outstanding contributions in research, is William C. Marshall.

A misstatement in this section in the Spring issue indicated that only two members of the ORNL staff have been selected to receive the E. O. Lawrence Award. Alvin Weinberg, Floyd Culler, C. R. Richmond, Arthur Upton, John Storer, and Milton Edlund, all at some time members of the ORNL staff, have been so honored.

Word has been received from the National Safety Council that Oak Ridge National Laboratory has once again earned the council's National Safety Award.

The Los Angeles Chapter of the American Society for Metals has established an additional major award for the 15th Annual Student Metallographic Contest, intended to recognize and encourage students to demonstrate their skill in producing a photomicrograph of a metal specimen from an energy-related field. It is called the ASM-William O. Harms Award.
Donald A. Gardiner was named Ordinary Member of the International Statistical Institute, which cited his “contributions to the development of statistical methods and his administration of statistical services.”

The American Ceramics Society has selected W. J. Lackey, Jr. as a fellow.
