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REVIEW

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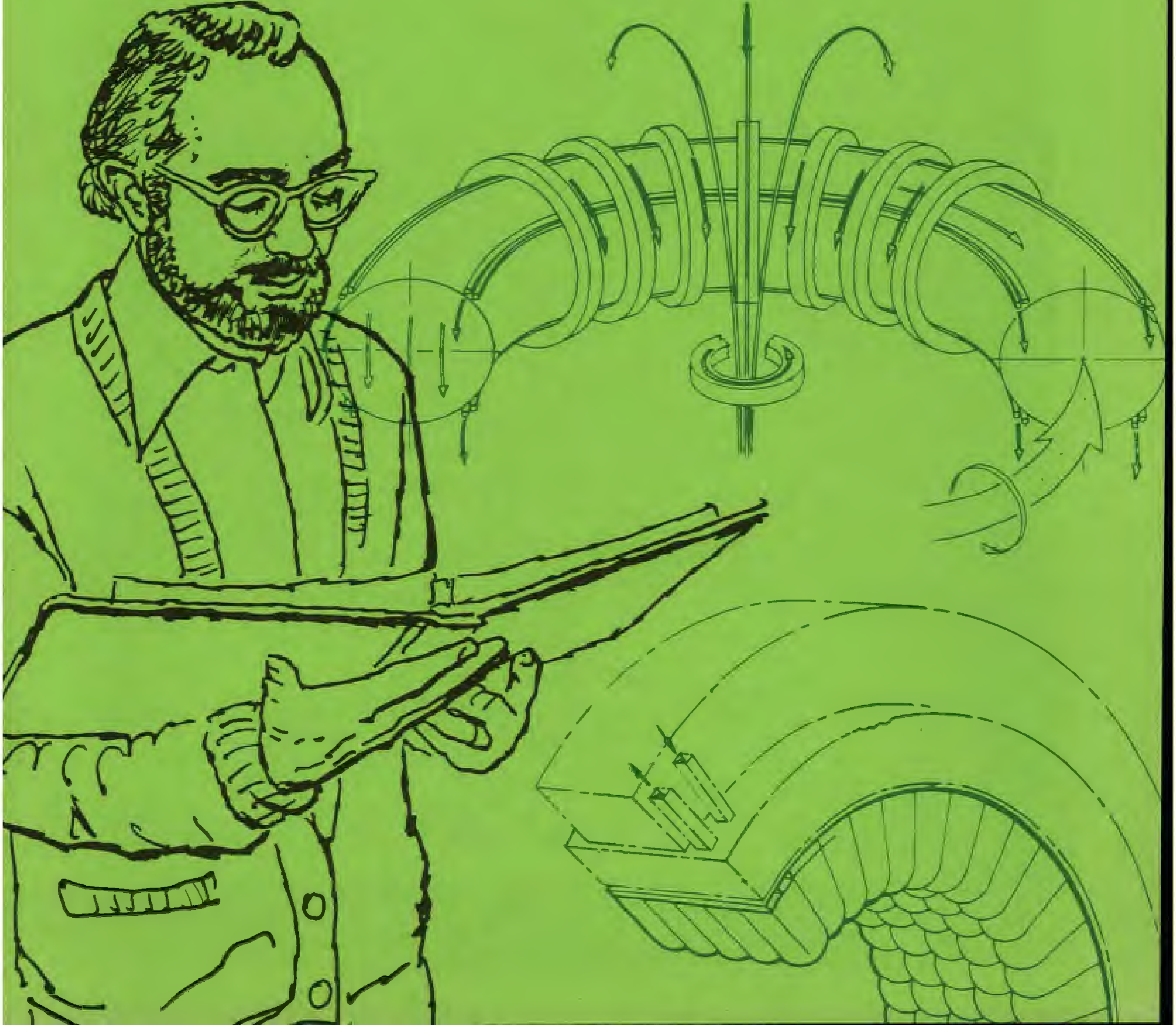

REVIEW

VOLUME 9, NUMBER 2 SPRING 1976

THE COVER: Getting it all together—including efficient designs for confining plasma, as in this Tokamak scheme, and for breeding tritium, as in this segment of a cellular blanket shown at bottom—is what it will take to make fusion feasible. Don Steiner, who coordinates fusion reactor studies at the Laboratory, tells us in this issue's lead article that fusion may be an important energy option in the next century despite environmental and economic question marks.

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FEATURES

OAK RIDGE NATIONAL LABORATORY

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If fusion reactors become feasible as a source of electricity, nuclear fusion may emerge as an important energy option in the next century. However, we should be warned that fusion will be neither cheap nor completely clean environmentally. This is the message of Don Steiner—a message he is ready to give at any time in print or on the podium. A native of Chicago, Steiner was educated mostly in Boston, where he earned his B.S. in chemical engineering and his M.S. and Ph.D. in nuclear engineering from MIT. In 1967 he joined the staff of ORNL's Reactor Division, and in 1968 he became involved in fusion problems at the suggestion of Dave Rose, at that time on leave here from MIT. In 1972, Steiner transferred to the Thermonuclear Division and was appointed director of the Fusion Reactor Technology Program, which coordinates fusion-related studies in seven divisions: Thermonuclear, Metals and Ceramics, Neutron Physics, Chemistry, Solid State, Chemical Technology, and Energy.


W. N. SHIPLEY

Fusion as an Energy Option

By DON STEINER

It has been my experience that there are four aspects of fusion power that are less than clearly perceived by members of the scientific, political, and public sectors: environmental issues, the role of alternative fusion fuels, economic potential, and time scale. Before anything else is said, I want to emphasize that I advocate an aggressive fusion program; however, the justification for such a program should be based not on wishful thinking, but on a realistic assessment of the potential of fusion power. Fusion power, although no panacea for our energy problems, may provide an important energy option for the next century.

A Point of Departure

Because it is generally acknowledged that fusion power will initially be based on a deuterium-tritium fuel economy, the emphasis of this article will be on D–T fusion reactors. However, the promise and prospects for alternative fuels will not be ignored.

The fusion of deuterium and tritium, two hydrogen isotopes, yields an alpha particle having an energy of about 3.5 MeV and a neutron having an energy of about 14.1 MeV. The neutrons so produced induce nuclear reactions in the structural materials of the fusion reactor, which results in substantial radioactive inventories. Thus, D-T fusion power has two important radiological considerations: It requires the handling of the radioisotope tritium, and it creates radioactivity.

The natural abundance of deuterium is so great that it poses no practical fuel resource limitations in a fusion power economy. However, the natural abundance of tritium is not enough to support such a power economy, and therefore it will be necessary to breed tritium in D–T fusion reactors. This is accomplished by neutron-induced reactions in a lithium-bearing blanket surrounding the plasma. Thus, the primary fuels in a D–T fusion economy are deuterium and lithium, and tritium is only an intermediate product.

In addition to tritium breeding, the fusion reactor blanket also serves the function of converting the kinetic energy of the fusion neutrons into recoverable heat. Nuclear power densities in fusion reactor blankets, limited both by plasma physics and materials considerations, will be one to two orders of magnitude lower than those in fission reactor cores.

Environmental Issues

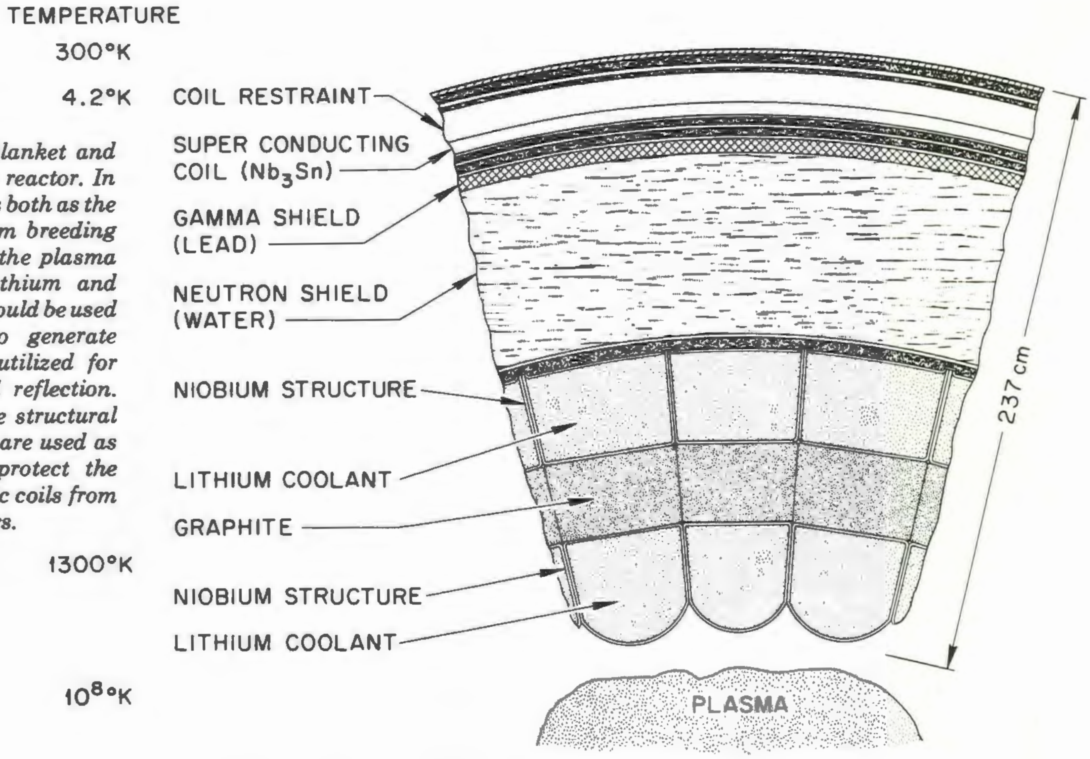
In assessing the environmental issues of fusion power, I shall consider the following topics: radioactivity in effluents under normal operating conditions, reactor safety and waste disposal, thermal effects, and resource requirements.

Routine releases. Under normal operating conditions, the greatest radiological impact of fusion power appears to be the release of tritium to the environment. Current estimates suggest that a 1000-MW(e) fusion power plant would have a tritium inventory of about 1 to 10 kg, or about 10^7 to 10^8 Ci. Because tritium permeates most metals at high temperatures, it can diffuse through containment walls, fluid piping, and heat exchanger tubing used for the blanket and its related systems. There are two primary paths by which tritium might eventually escape to the environment during normal operating conditions—through the blanket containment walls and fluid piping into the surrounding atmosphere or through the coolant system into the steam cycle via the coolant-steam heat-exchanger tube walls.

There are, as yet, no generally applicable standards concerning tritium release; nor can we say what the future limitations on tritium releases from fusion reactors should be. However, if light-water fission reactor guidelines are applied to fusion reactors, the tritium containment in the blanket and associated fluid piping and heat-exchanger tubing will have to approach 99.9999%. Although this degree of containment seems technologically feasible, a major objective of fusion reactor technology will have to be the demonstration of tritium containment at acceptable costs. Moreover, standards concerning tritium release will have to be established in the context of future fission and fusion power systems. To this end, a more precise understanding of the physical, chemical, and biological behavior of tritium in the environment is needed.

Reactor safety and waste disposal. The magnitude and characteristics of the radioactive inventories induced by neutron interactions in the structural material of the blanket are major considerations in assessing fusion reactor safety and radioactive waste disposal. For the wide range of materials and blanket designs being considered, the level of induced activity at equilibrium is generally in the range of about 10^9 to 10^{10} Ci for a 1000-MW(e) plant, clearly a significant level. However, the level of activity by itself is not a meaningful measure of the technological problems posed by radioactive inventories; evaluation of the associated nuclear afterheat and examination of the time-dependent behavior of the activation products are also necessary.

At shutdown the afterheat power density in the fuel of advanced fission reactors is anticipated to be at least one to two orders of magnitude greater than that expected in the structural components of fusion reactor blankets. The conclusion is that afterheat removal will be less of a problem in fusion reactors than in fission reactors. Moreover, it appears that the engineered safety features necessary to limit



This is a segment of a blanket and shield region of a fusion reactor. In this design, lithium serves both as the coolant and as the tritium breeding medium. Neutrons from the plasma are absorbed by the lithium and converted to heat, which could be used for producing steam to generate electricity. Graphite is utilized for neutron moderation and reflection. The niobium provides the structural support. Lead and water are used as shielding materials to protect the superconducting magnetic coils from neutrons and gamma rays.

biological impact in the event of an accident may have to satisfy less stringent requirements in fusion reactor design than in fission reactor design. This observation does not mean that fusion reactors will necessarily be safer than fission reactors, but rather that the technology and engineering necessary to achieve a given level of safety may prove less difficult and costly for fusion reactors.

A number of materials are candidates for fusion reactor structure. These include refractory alloys based on niobium and vanadium, as well as conventional iron-base and nickel-base alloys. Calculations suggest that, if niobium-base materials are used, long-term solutions to waste disposal similar to those sought for radioactive wastes from fission reactors may be required. On the other hand, the use of materials such as vanadium-base alloys might allow recycle of the blanket structure following a relatively short (less than 10 years) cooling period. Recycle of iron- and nickel-base structures might also be feasible, but the required cooling period would be at least 50 years. Within this context, it is possible that a fusion power economy might eliminate the need for long-term solutions to the radioactive waste disposal problem.

Thermal effects. The D–T fusion reaction releases energy in two forms—neutron and charged-particle energy. The neutron energy, which eventually is manifested as heat within the blanket, would be recovered by a thermal energy conversion system. The charged-particle energy could also be recovered as heat by means of a thermal energy conversion system. However, direct recovery of this portion of the energy may also be possible. For example, R. F. Post of the Lawrence Livermore Laboratory has proposed an electrostatic scheme for converting the kinetic energy of charged particles directly into electricity. In this scheme, the charged particles that escape from the plasma confinement region would be slowed down by electrical fields and would be collected on high-voltage electrodes, rather like operating a particle accelerator in reverse.

Because only about 20% of the energy released in D–T fusion appears as charged-particle energy, the impact of such direct energy conversion is marginal. For example, consider a case in which a thermal energy conversion system of 40% efficiency is used for recovery of the neutron energy and a direct energy conversion system of 70% efficiency is used for recovery of the charged-particle energy. The overall recovery efficiency for such a system would be 46%, about 15% higher than that for the thermal conversion system itself. However, energy conversion is not the total energy cycle in fusion reactors. Fusion reactors will inherently require input power to establish the fuel conditions necessary for fusion power production. Therefore, a fraction of the gross electrical output of the plant must be recirculated to sustain the fusion process. The amount of recirculating power required in fusion power plants can be appreciable. Thus, even when direct energy conversion is assumed for a portion of the fusion energy release, the overall plant efficiency (that is, the ratio of the net electrical power output to nuclear power release) of current fusion reactor concepts is comparable to the overall plant efficiencies of fossil and fission power plants (i.e., in the vicinity of 30 to 40%), and there are corresponding thermal effluents as well.

Resource requirements. The use of deuterium and lithium for fusion power should result in environmental impacts and economic constraints that are less stringent than those associated with the fuel requirements in fission power plants. On the other hand, the resource requirements in construction of the fusion reactor plant seem to be considerably more extensive. This is because nuclear power densities in fusion reactor blankets are inherently lower than those in fission reactor cores, which means that, for a given power generation level, a fusion reactor blanket will require significantly more structural material. Although there do not appear to be any resource limitations that would prevent fusion power development, the economic and environmental implications of the construction resource requirements must be examined carefully.

Alternative Fusion Fuels

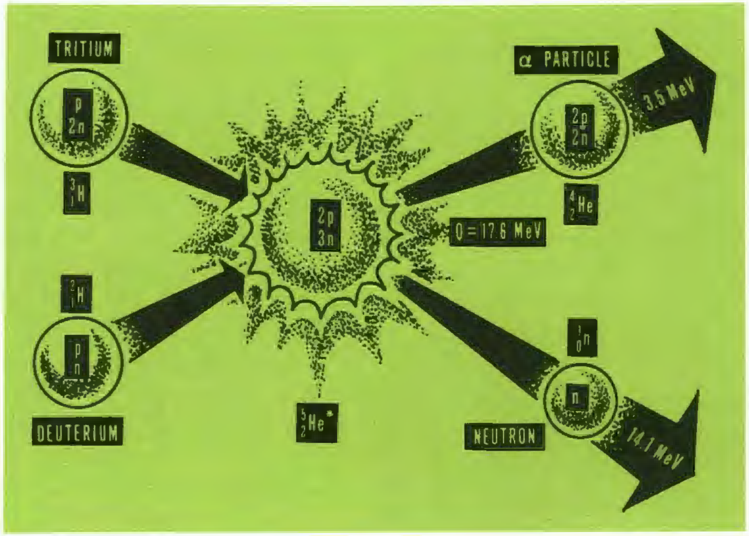
Several environmental drawbacks are commonly attributed to D-T fusion power. First, it produces substantial amounts of neutrons that result in induced radioactivity within the reactor structure, and it requires the handling of the radioisotope tritium. Second, only about 20% of the fusion energy yield appears in the form of charged particles, which limits the extent to which direct energy conversion techniques might be applied. Finally, the use of D-T fusion power is limited by lithium resources, which are less abundant than deuterium resources (this limitation is on the time scale of about 1000 years).

These drawbacks of D-T fusion power have led to the proposal of a number of alternatives—for example, fusion power reactors based only on deuterium. Such systems (1) reduce, by about an order of magnitude, the production of neutrons and accordingly the need to handle tritium; (2) produce more fusion power in the form of charged particles; and (3) are not limited by lithium resources. It has also been suggested that materials with higher atomic numbers (such as lithium, beryllium, and boron) be used as fusion fuels to provide power that is essentially free of neutrons and tritium and that releases all of its energy in the form of charged particles.

Although such alternatives to D-T fusion power are attractive, there is an important scientific caveat. To derive useful amounts of power from nuclear fusion, it will be necessary to confine a suitably dense plasma at fusion temperatures (10^8 °K) for a specific length of time. This fundamental aspect of fusion power was first quantified by the British scientist, J. D. Lawson, who formulated a convenient expression for the product of the plasma density, n, and the energy confinement time, τ, required for fusion power breakeven (i.e., the condition at which the fusion power release equals the power input necessary to heat and confine the plasma). Lawson showed that the required product, $n\tau$, depends on the fusion fuel and is primarily a function of the plasma temperature. Of all the fusion fuels under current consideration, the deuterium-tritium fuel mixture requires the lowest value of $n\tau$ by at least an order of magnitude and the lowest fusion temperatures by at least a factor of 5. When the plasma requirements for significant power generation are compared with the anticipated plasma performance of current approaches to fusion power, it is apparent that fusion power must initially be based on a deuterium-tritium fuel economy. Moreover, it is my opinion that the implementation of alternative fuels will require the evolution of novel approaches to fusion power.

As a final point it should be noted that the potential of fusion-fission (hybrid) concepts is

Here is a fusion reaction in which nuclei of tritium and deuterium fuse, resulting in release of an alpha particle (helium nucleus) and an energetic neutron. When the neutron is captured, its energy will be converted to heat.



also under study. In such concepts, fusion-produced neutrons are used to generate fission power and breed fissile material in the blanket surrounding the plasma. The fission power produced in hybrid concepts relaxes the required plasma performance significantly, but introduces the complexities and additional costs of fission fuel cycles. The eventual role of such concepts in a nuclear power economy is yet to be quantitatively assessed. However, I believe that hybrid concepts cannot compete economically with fission breeders and that they negate the major environmental and societal advantages attributed to fusion power.

Power Generation Costs

Power generation costs are generally divided into three components: capital costs, fuel costs, and operation and maintenance costs. For example, light-water fission reactor power generation costs are presently distributed as follows: About 70% capital costs, about 20% fuel costs, and about 10% are operation and maintenance costs. Fission power generation is said to be highly "capital-cost intensive;" that is, the power cost is to a large extent determined by capital-cost investment and to a lesser extent by fuel costs. This is even more the case with fusion reactors. It appears that about 90% of the power generation cost for fusion reactors will be capital expenditures and about 10% will be operation and maintenance; the fuel cost of fusion power should be less than 1% of the total. In this context, it is of interest to note that solar power will also be highly capital-cost intensive because there are no fuel costs.

Current estimates place fusion capital costs above fission capital costs by at least a factor of 2, a differential that reflects the lower nuclear power densities of fusion power systems. On the other hand, fusion fuel costs will be lower than fission fuel costs. Operation and maintenance costs should be comparable for both. On the basis of current costing procedures, fission power appears to be less expensive. However, if, as expected, environmental and societal costs in their broadest sense become an important factor in determining power generation costs, then fusion power should be economically attractive. In the long term, both fusion and fission power must compete with solar power, which, under current costing assumptions, is more expensive than either. The economic viability of fusion and solar power will rest largely on the effect environmental and societal costs have on power generation costs.

Time Scale

To assess the time scale required for fusion power development, it is first necessary to define the critical steps in a fusion power development program. To this end, let us consider the program being proposed by the ERDA's Controlled

Thermonuclear Research Division. In this program plan, the major goal is the operation of a Fusion Power Demonstration Reactor (DEMO), whose objective is to demonstrate that fusion power is safe, reliable, and, in principle, economically competitive with alternative energy sources. The DEMO would be preceded by at least two key experimental devices. The first of these called the Fusion Test Reactor, would demonstrate fusion energy production from the burning of deuterium and tritium. For example, the Tokamak Fusion Test Reactor, scheduled to be operational around 1980, is expected to cost more than $200 million, including contingency and escalation. This would be followed by the Experimental Power Reactor (EPR), which would demonstrate the basic components and systems of a fusion power reactor. It is not yet clear whether or not an intermediate device would be required between the EPR and the DEMO, but for the purposes of this discussion, let us assume that there are three critical devices: the Fusion Test Reactor, the Experimental Power Reactor, and the Demonstration Power Reactor.

Clearly, any assessment of the fusion power time scale must be based on the assumption of favorable progress in the areas of plasma physics and technology. Given such a basis, the fusion power time scale will be affected by the level of funding, the time required to design and build large devices, and the amount of time each device must operate to establish the confidence to move on to the next stage. It is my judgment that, even if funds for the program were not limited, the DEMO could not be operated before the end of this century. This I regard as the minimum *credible* time scale for the DEMO; I think that the minimum *practical* time scale would yield an operational DEMO sometime between the year 2000 and the year 2010. I emphasize that this eventuality assumes continued success in the areas of plasma physics and technology and is predicated on a level of funding commensurate with the required experimental and technological programs.

Concluding Remarks

It is common for advocates of the long-term energy sources (fission, fusion, and solar) each to promote his source as the ultimate solution to man's energy needs. I believe that such a stance is divisive and cannot lead to a rational energy policy. Although I am a fusion advocate, I would encourage a long-term energy policy that has as its goal the development of fission breeders, fusion, and solar energy. I believe that, since all three energy sources might be used effectively, it would be highly desirable to have energy options rather than to be totally reliant on a single energy source. In this context, fusion deserves vigorous funding and very active pursuit not because it is a guarantee for "clean, limitless, and cheap power," but rather because it may provide an important energy option for the next century.

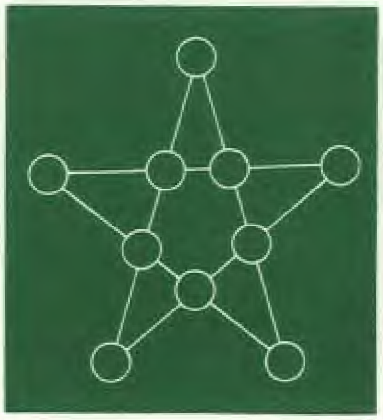
Staff quote:

"It should be carefully noted that successful preservation of embryos of various mammalian species now increases the likelihood of attempts to freeze human embryos as well. Several European investigators are showing interest in that possibility because freezing could improve the chances of successful human ova transfer, which would help physicians circumvent tubal blockages causing infertility. It is estimated that more than 25% of infertile women (who comprise about 5% of the total female population of child-bearing age) suffer from tubal blockages resulting from various causes, including gonorrhea, now reaching epidemic proportions.

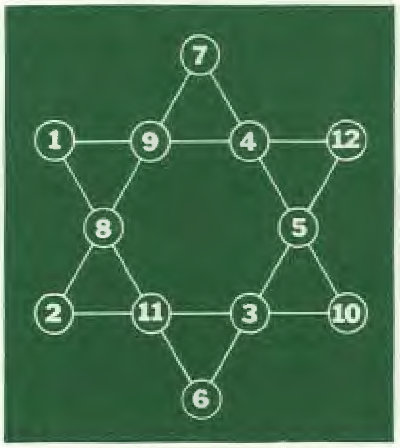
The ovum transfer technique consists of inducing a woman to superovulate by hormonal stimulation and surgically removing her ova, which are then fertilized in vitro, cultured for about 48 hr, and transferred back into her own uterus . . . . Freezing of fertilized ova offers an obvious alternative, since it would permit storage of the embryos for the several months required for the woman's physiology to return to a normal state."—**S. P. Leibo,** *commenting on an October 1975 meeting of the British Society for Low Temperature Biology held in London.*

Take A Number.....

By V. R. R. Uppuluri



6	1	8
7	5	3
2	9	4



"MAGIC" STARS

In general, it is nontrivial to show that a proposition is impossible. One such result is the impossibility of a five-pointed "magic" star.

A lot is known about magic squares. For instance, one can easily write a magic square of order three, using the numbers 1, 2, . . . , 9. In such a square, each row sum, each column sum, and each sum across the diagonals is equal to 15.

Similarly, one can write down a six-pointed "magic" star, using the numbers 1, 2, . . . , 12. As seen from the figure, the sum of the four numbers along any line is equal to 26. It can be proven, however, that it is impossible to have a five-pointed "magic" star, using the numbers 1, 2, . . . , 10. One proof by William Pruitt uses the idea that, for a five-pointed magic star to exist, the numbers 1 and 10 would have to be on the same line; he then proceeds to show that, if such a star did exist, then on no line in the star would there be two numbers whose sum is 11. Thus, a five-pointed "magic" star using the numbers 1, 2, ... , 10 is impossible.

The author conjectures that there can be no "magic" stars with an odd number of vertices.

LARGEST KNOWN PRIME NUMBER?

A natural number is said to be a prime if the only divisors of that number are itself and unity. In 1971, Bryant Tuckerman discovered $2^{19937} - 1$ to be a prime. This is a number with 6002 digits.

Silhouette of huts in a Zulu village.

Springbok Science

Chemistry on the Dark Continent

By JERRY BRAUNSTEIN

Jerry Braunstein has been conducting research for 18 years on the molten salts and concentrated aqueous electrolytes that have application to high-temperature batteries, fuel cells, geothermal systems, and hydrogen generation systems. Last summer he presented his views on the relevance of molten salt science to energy production at the Conference of the South African Chemical Institute, where he was one of two foreign guest lecturers. In return, he had some memorable experiences in South Africa, ranging from apartheid to Zulu dancing. Braunstein, who holds a doctoral degree from Northwestern University, came to ORNL in 1966 from the University of Maine, where he had been Professor of Chemistry. Author of about 70 papers in the areas of electrolyte physical chemistry and theoretical chemistry, he is coeditor of *Advances in Molten Salt Chemistry* and a faculty member of the University of Tennessee–Oak Ridge Graduate School of Biomedical Sciences.

Favored topics of conversation while munching *boerworst*[1] at a *braai*[2] in the *bundu*[3] were Chaka's[4] modification of the *assegai*[5] and the military strategy of the 1820 settlers[6] and *voortrekkers*.[7] The *braai* took place one weekend last July on a beach north of Durban, Natal, following the 1975 Conference of the South African Chemical Institute (SACI). My contacts with South African chemists, until that time, had been quite limited. I had met Hugh Brookes, of the University of Natal, at a Gordon Research Conference on Molten Salts several years ago and had been external examiner for the thesis of one of his doctoral students. John Bayles, head of the Chemistry Department of the University of Natal, visited Oak Ridge about two years ago for discussions in the field of electrochemistry of concentrated aqueous

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[1] Afrikaans farmer's sausage.

[2] Barbecue, or cookout (Afrikaans).

[3] Back-country, boondocks (Zulu).

[4] Zulu chief from about 1820 to 1830.

[5] African native spear. Chaka replaced the throwing spear with a short, stabbing spear, which revolutionized warfare among the Zulu tribes, contributing to the dominance of Chaka's tribe.

[6] English settlers in the Port Elizabeth area of South Africa (roughly equivalent in social significance to passengers on the Mayflower).

[7] Boers, of Dutch and Huguenot ancestry, who migrated northward from the Port Elizabeth and Capetown areas to the interior highlands of South Africa during the nineteenth century to escape dominance by the English-speaking settlers; roughly equivalent to pioneers.

D. DUDENBOSTEL

electrolytes and molten salts with Milt Lietzke, Bill Marshall, Bob Mesmer, and me.

About a year ago, John, as chairman of the 1975 SACI Committee, recommended that I be invited as one of two foreign guest lecturers at the conference and that I follow the conference with a three-week lecture tour of South African universities and research laboratories. (The other invitee was Professor Guy Ourrisson, an organic chemist from the University of Strasbourg, France.) Despite my scientific interest in visiting the conference and laboratories and a great sociological interest in touring Africa, I had mixed feelings about going because of South Africa's apartheid policy; but curiosity, both scientific and sociological, overcame my misgivings and I accepted the invitation.

Although I was not aware of any large-scale molten salt programs in the country, there was enough interest and activity in the field, not only at the University of Natal, but at several of the government laboratories, to enable me to make valuable scientific contacts during the trip that would have been impossible otherwise.

The trip started with a grueling 15-hr direct flight from New York to Johannesburg with a half-hour refueling stop in the Cape Verde Islands, which had been liberated from Portugal about a week earlier. About half the passengers on the nearly full Boeing 707 were returning South African AFS students who seemed to have thoroughly enjoyed their stay in the United States. My seatmate was an American who had lived in South Africa for several years and now considered it his home.

It was a warm day in July, although the season was winter, when John Bayles met me at the airport in Durban on the Sunday before the conference. After a brief drive around the city, which is the largest port in Africa, John dropped me at the University Residence, where most of the attendees at the conference, which was scheduled to start the next morning, were staying.

Costumed women dance to the rhythm of a horn, played by their leader, in a Shemba religious ritual.


J. BRAUNSTEIN

About 150 people from all parts of South Africa attended. Although South Africa is officially bilingual (English and Afrikaans), most of the papers were in English. Most papers dealt with organic chemistry, natural products chemistry, polymer chemistry, and other topics related to South African industries and resources. The physical and inorganic papers were heavily oriented towards instrumental applications, analysis, and structure determination (e.g., x-ray crystallography, chromatography, some electron spectroscopy for chemical analysis). Also, some papers were understandably slanted towards South African natural products, both organic, such as coal, plant, and animal extracts, and inorganic, including uranium, gold, platinum, chromium, and diamonds. The air of prosperity in the country, at least among whites, is remarkable. South Africa has an abundance of almost all resources (including low-sulfur coal) except oil (some offshore exploration is under way), bauxite (which is imported now for the aluminum industry, although some development of less concentrated aluminum minerals is under way), and fresh water.

At the conference I delivered a public lecture, "Hydrogen: Key to Synthetic Fuels" and a plenary lecture, "Applications of Molten Salts in the Development of Energy." Carlos Bamberger and I had just published a review on the first topic in *American Scientist* (see Winter 1976 issue of ORNL *Review*). In both the review and my lecture, I discussed the potential of large-scale hydrogen production as a fuel to replace natural gas, as well as its importance in (1) the more efficient use of fuels and primary energy sources, (2) energy storage, (3) transportation, and (4) the chemical, metallurgical, and fertilizer industries. I also reviewed research on improved methods of hydrogen production.

The second talk (which is the subject of a future review for *American Scientist*) dealt with (1) the importance of molten salts in energy conversion, distribution, storage, and conservation in the light of the special characteristics of molten salts and (2) the structural features that confer these characteristics. I also discussed theoretical and experimental methods for investigating molten salt properties.

I gave these lectures during my visits to such universities and research institutes as the University of Natal, University of Port Elizabeth, National Chemical Laboratory, National Institute of Metallurgy, and Atomic Energy Board. At the University of Natal, I also gave a research seminar on "Transport and Thermodynamics in Molten Salts and Concentrated Aqueous Electrolytes," in which I discussed my current research in this area in greater detail than in the review lectures.

The convention I attended was held at the University of Natal in Durban. This is a relatively new university, having a student body of about 5000; classes are conducted in English. The Chemistry Department is in a well-equipped five-year-old building. As in most South African universities, faculty teaching loads are usually heavy due to the trend of decreasing numbers of advanced chemistry students and increasing demands for service courses for engineering students. I was surprised at the relatively large number of American chemists, hit by the early 1970s depression, working in South Africa now.

J. BRAUNSTEIN

Adorned with headbands and white fur pieces, this team of N'goma Zulu dancers prepares to do a tribal dance in the Durban competition.

The University of Port Elizabeth is a small new university having about 2000 students; about half of the departments (including Chemistry) conduct classes in English, whereas the rest (including Physics) give instruction in Afrikaans. Some universities use only the Afrikaans language. In an effort to avoid scientific isolation, funds for foreign travel to meetings, short leaves or longer sabbatical leaves, and visits of foreign guests are very liberal at South African universities and research laboratories. Most of the scientists I met had just returned from, or were preparing to leave for, meetings or extended stays at European or American research establishments.

The Atomic Energy Board is located at Pelindaba (near Pretoria), a Sotho tribal place whose name signifies "where we stop talking and start working." Beyond a hill, the stacks of Valindaba (meaning "this, we don't talk about"), the uranium isotopes separations plant, were pointed out to me, but no visit was offered. (Nor requested. Two days earlier some of the more flamboyant newspapers had displayed such headlines as "CIA TRYING TO STEAL OUR URANIUM SECRETS!") The Atomic Energy Board, which has about 3000 employees (about a third of whom have technical degrees), apparently has no extensive breeder reactor programs, possibly because uranium ore is a cheap by-product of South African gold extraction. The Board shows considerable interest (although little discernible activity) in molten salt reactors because of South Africa's extensive thorium resources. The molten salt discussions, which occupied most of my time there after my talk (I was told that it was 10 years to the day after Alvin Weinberg had spoken at the dedication of their ORNL Research Reactor-type SAFARI reactor—and Alvin is a hard act to follow, even after 10 years), pertained to basic programs, but with special attention given to the materials and metallurgical problems at the Atomic Energy Board.

During the lecture tour following the conference, I visited molten salt research programs under way in several different areas and exchanged views on recent developments. At the University of Natal, Hugh Brookes (who was on sabbatical in England at the time) had a program on electrochemical measurements of thermodynamic properties of molten nitrate mixtures designed to test models of molten salt solutions. John Bayles was in the process of setting up a rotating electrode for studies of electrochemical and mass transport properties of molten salts. Hugh Brookes and Lyn Simmons (a displaced Texan) had initiated temperature-jump measurements for kinetics studies in molten salts. At the National Physical Laboratory in Pretoria, there has been interest in electrolysis of molten silicates for modifying the composition of glasses for special optical properties. At the Atomic Energy Board, also in Pretoria, the exchange of ions between a molten salt and a glass has been under investigation by Dr. de Wet, director of the Board's Chemistry Division. He is trying to understand the relation between the thermodynamic properties and the rate of migration of ions in mixed alkali ion glasses. Another molten salt program at the Atomic Energy Board focuses on the use of molten cyanides and liquid alloys for the extraction and separation of the platinum group metals. The principle of the separation is not unlike that of the proposed fuel processing scheme for the molten salt breeder reactor. Dr. Karl Fouche's group has been engaged in electrochemical and spectroscopic studies of the species present in the solutions of the platinum group cations in molten cyanides. At the National Institute of Metallurgy, in Johannesburg, which had at one time been part of the Atomic Energy Board, there is a program aimed at the development of molten salt electrolytic methods for the recovery of base metals such as lead and zinc; another program explores the feasibility of molten salt electrolysis for refining ferrochrome alloys. Thus, South Africans are studying a fairly diverse range of topics in molten salt chemistry although not on a very large scale.

Weekends and spare time permitted me some interesting views of South Africa. Highlights included the spectacular view of Table Mountain at Capetown (where my host was Dr. Max Peisach, of the Southern Universities Nuclear Institute, who has many friends in Oak Ridge), the magnificent Indian Ocean beaches of Durban, and a trip to the Hluhluwe game preserve in Zululand arranged by John Bayles. Among the animals we saw and photographed in their natural habitats were zebra, white rhinoceros (which are not white), gnu, springbok (this graceful South African gazelle is, so to speak, the bald eagle of South Africa, its national emblem), crocodile, baboons, and hippopotami.

During the week of the conference, the mayor of Durban, resplendent and imposing in ceremonial uniform, held a reception at the City Hall for convention participants. His greeting to us included a few words in Afrikaans, with which he was apparently somewhat ill at ease since Durban is a predominantly English-speaking city. (A standing joke among some Durbanese is that, although the Queen is unaware of it, Durban is England's last remaining colony.)

The weekend following the conference allowed time for a cookout with some South Africans and other Americans on a beach north of Durban, where we did not swim because of the absence of shark nets. I did swim at the net-protected Durban city beach—the winters are reputed to be more pleasant than are the steamy summers. I also had the opportunity to see a fascinating competition of N'goma Zulu dance teams on a Saturday afternoon in Durban. These groups of amateur dancers, sponsored by their employers in the manner of bowling teams in the United States, perform nearly every week. Local, regional, and national competitions are held. The fantastic, yet disciplined, dances are adaptations and syntheses of traditional Zulu tribal dances. Among the dances of Zulu mine workers, for instance, we admired the "gumboot dance," in which elaborate steps were featured to the accompaniment of a complicated rhythm created by slapping rubber hip boots that are worn by the workers in the mines.

My introduction to South African apartheid came through the separate airport restaurant and rest room facilities; to American and European visitors, the system appeared, at best, cumbersome. As a superficial example, one European later told us that he nearly missed a plane connection because he saw so many signs reading "Blanke" (white) and "Nie Blanke" (nonwhite) that he could not find the "Departures" sign.

The South Africans I met exhibited genuine friendship for Americans. Many pointed out parallels in the histories of the United States and South Africa in terms of dates of settlement of Europeans, heterogeneity of population, and the South African Trek (migration from the South coastal to the interior highland areas) vs the American "Winning of the West."

The exchange of views, both scientific and nonscientific, especially in the context of the South African environment, was invaluable and could not be matched even by frequent encounters with South African scientists at American and European meetings.

JIM RICHMOND

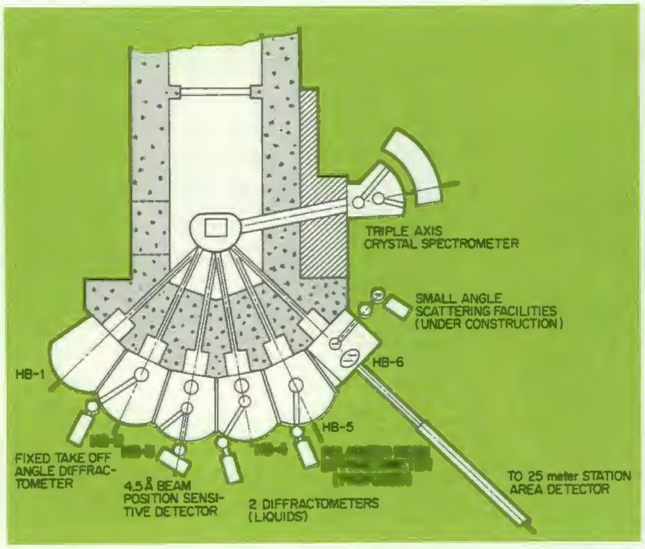
For 27 years, Wally Koehler has studied the nature of matter by examining the scattering of neutrons by solids. The application of neutron scattering to solid state physics started at ORNL 30 years ago, making 1976 a year of celebration for Koehler's colleagues, climaxed by an international conference here in June. From 1942 to 1948, Koehler worked for the Manhattan Project at the University of Chicago, from which he earned his B.S. and M.S. in physics. In 1953, four years after coming to ORNL, Koehler received the Ph.D. in physics from The University of Tennessee. At ORNL he has served as group leader in neutron diffraction and section chief in crystal physics in the Solid State Division. He has taught physics at the Virginia Polytechnic Institute and in the Oak Ridge Graduate Training Program, and he is the author or coauthor of about 120 papers. He spent 1958–59 at the University of Grenoble in France, where he was both a Fulbright and a Guggenheim Fellow. He is shown here interacting with his triple-axis, polarized-beam spectrometer at HFIR.

Neutron Scattering at ORNL ...a History

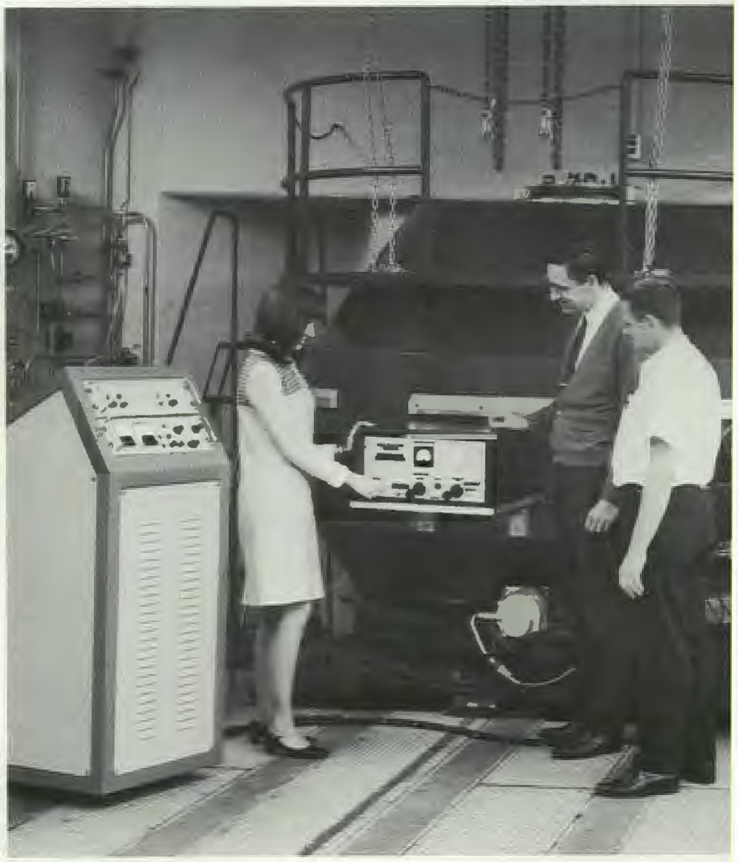
By W. C. KOEHLER

To those of us in ORNL's neutron scattering programs, 1976 is a special year as well as the bicentennial anniversary of the nation because it marks the 30th anniversary of the first application of neutron scattering to the study of solids and liquids. In 1946, E. O. Wollan and C. G. Shull, using the then intense neutron beams at the Oak Ridge Graphite Reactor, opened the door to a whole new field of physical research. Although the field has developed and changed drastically since those first experiments, the fundamentals on which it rests were first laid down in those early days at the Graphite Reactor.

Because of ORNL's important role for 30 years in applying neutron diffraction methods to solid state physics, it is appropriate that an international Conference on Neutron Scattering will be held this June in Gatlinburg under the sponsorship of ORNL and ERDA. The conference encompasses a wide range of applications of neutron scattering to the study of condensed matter—from chemical



Neutron scattering facilities of the ORR—existing and planned. Specialized instrumentation is being installed to supplement the equipment of the HFIR and to extend the range of problems that can be studied at the Laboratory.



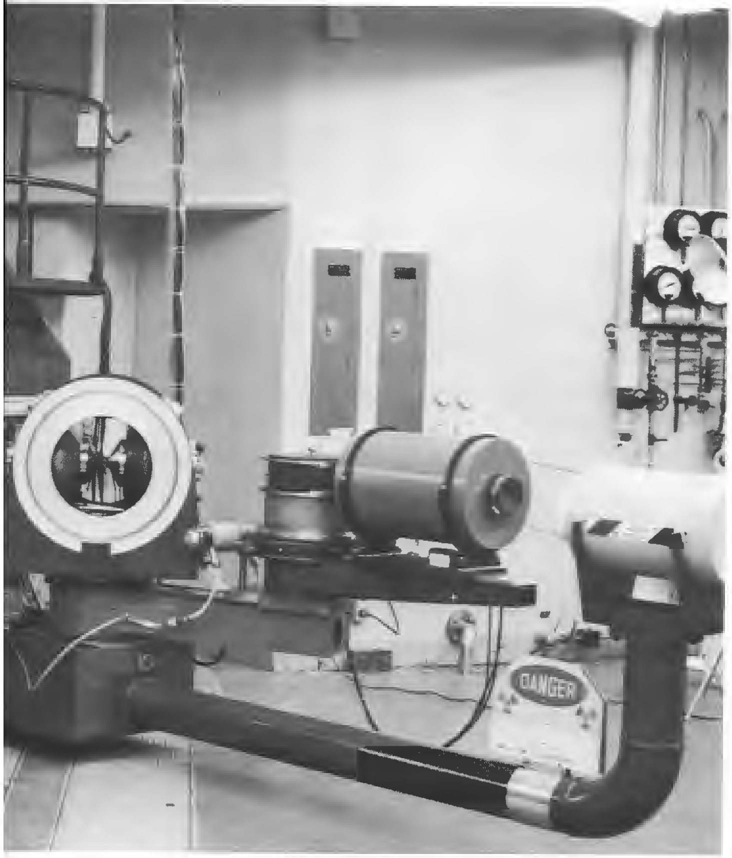
B. K. NORRIS

crystallography to neutron interferometry, from crystal field spectroscopy to the dynamics of quantum liquids. Conferees will include representatives from Canada, England, Norway, Sweden, Denmark, Germany, Switzerland, France, and Austria. Also expected are a large delegation from the Institut Laue-Langevin (the joint French-German-English establishment at Grenoble) and scientists from Japan, India, Pakistan, the Soviet Union, Hungary, Poland, and Australia. American representatives will include scientists from the national laboratories, the Reactor Center at the National Bureau of Standards, and universities such as the Massachusetts Institute of Technology (MIT), University of Missouri, and Georgia Institute of Technology.

Neutron scattering had its origin in 1932, the year that marked the discovery of the neutron by Chadwick. Even its prehistory is well defined, for 1924 was the year of de Broglie's paper, from which the wavelike properties of the neutron were recognized. The pre-reactor period is subdivided according to the types of neutron sources in existence at the time. What may be called the early pre-reactor period was an exciting one for physics in general and for neutron physics in particular. The first demonstration of Bragg scattering or diffraction of slow neutrons was carried out during this period. Because of the very low intensities and polychromaticity of howitzer neutrons, experimental investigations of crystal diffraction effectively ended with the demonstration of the effect.

This early pre-reactor period was notable for intense activity in the area of magnetic scattering of neutrons, much of which was initiated by a suggestion by Felix Bloch. There was at the time good theoretical reason to believe that the neutron had a magnetic moment of the order of one or two nuclear Bohr magnetons, and Bloch proposed a method of measuring the neutron moment by means of the magnetic interaction of slow neutrons with magnetized materials. Shortly thereafter, the experimentalists detected the phenomenon of neutron polarization, and estimates of the magnitude and sign of the neutron magnetic moment were announced. But here again, limitations of the source prevented any but qualitative experimental results.

Perhaps the most fruitful developments of this period were in theoretical investigations. In his original paper Bloch chose a particular form for the magnetic interaction that was equivalent to representing the neutron as a simple magnetic dipole. In a subsequent and more detailed calcula-

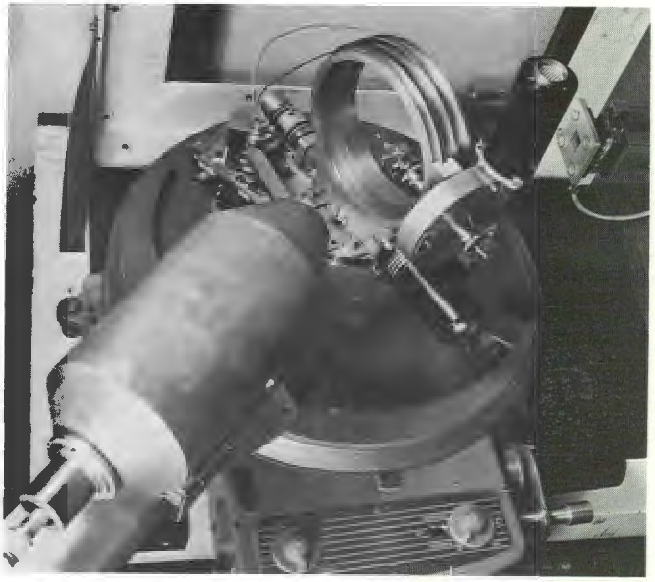


The polarized beam spectrometer at HB-1 of the HFIR. Ralph Moon and Jim Sellers observe Sharon King, who did most of the programming to control the instrument, as she adjusts an rf spin reversal circuit.

tion, Schwinger adopted a point of view that was equivalent to representing the neutron by an amperian current. (The choice of representation can be related to the question of whether the neutron senses the magnetic induction, B, or the field intensity, H, in a magnetic medium.) Bloch showed that it should be possible experimentally to distinguish the two cases, but again, because of low intensities, a definite answer was not forthcoming until modern times.

It was then that the first of three major theoretical papers, now classics, by O. Halpern and his colleagues, as well as the earliest theoretical studies of the inelastic scattering of neutrons, appeared.

The late pre-reactor period extends from about 1939 to 1942. This period was noted for the development of the pulsed cyclotron technique for producing higher fluxes of neutrons than those previously available and there was initiated the now well-known series of experiments on total neutron cross sections. For condensed matter applications, the measurements by Alvarez and Bloch of the neutron magnetic moment should be cited. They eventually used cyclotron neutrons and a resonance technique with a neutron polarizer and analyzer. In this period appeared the second and third of the Halpern trilogy, which for a long time served as the theoretical foundation of thermal neutron scattering from condensed matter.



The four-circle diffractometer installed at HB-4 of the ORR for high-resolution crystallography. The monochromatic beam comes up vertically by scattering through 90°. This instrument is still in use by Al Narten in studies of the structure of liquids.

The reactor period began when, in December 1942, the first nuclear reactor was successfully operated under the west stands of the University of Chicago athletic field. The following year the Oak Ridge Graphite Reactor went into operation, and in 1944 Chicago Pile 3, a heavy-water reactor, was started up in a forest preserve south of Chicago. For the first time relatively copious fluxes of neutrons, of the order of 10^{11} to 10^{12} neutrons cm^{-2} sec^{-1}, were available for experimentation; it is at these reactors that the modern phase of neutron diffraction can be said to have begun.

The first applications of neutron diffraction were to the design and construction of neutron crystal spectrometers for use as energy selectors for thermal neutrons. Significant data had been obtained from such instruments, both at Oak Ridge and at Argonne (some as early as 1944), but this work was not declassified until 1946.

In November of 1945, Wollan set up a double-crystal spectrometer at the Graphite Reactor; the second crystal component was an instrument that he had used in his earlier researches in x-ray physics at the University of Chicago and which, incidentally, is now on exhibit at the Smithsonian Institution. He found large intensities in the reflected beam from rock salt single crystals, but he was disturbed by the fact that different crystals, and indeed equivalent orientations of the same crystals, gave inconsistent results.

In April of 1946, the first neutron powder pattern, again of rock salt, was recorded with "sufficient intensity that quite satisfactory powder lines [could] be observed." The monthly progress report of this period goes on to say, "This eliminates difficulties with extinction and with orientational irregularities which were encountered with single crystals and opens up possibilities for investigating many elements and compounds which cannot be procured in single crystal form."

In August of 1946, C. G. Shull, now at MIT, came to the Laboratory, and between 1946 and 1948 the fundamentals of nuclear scattering of thermal neutrons by crystalline powders were systematically investigated at Oak Ridge by Shull and Wollan. Both of these physicists, having strong backgrounds in x-ray physics and x-ray diffraction techniques, recognized the potentialities of neutron diffraction for application to nuclear and solid state physics. But recall, if you will, that nuclear amplitudes, unlike x-ray scattering amplitudes, are quantities that had to be determined experimentally. Before the first amplitude could be measured with confidence, it was necessary to study and to untangle the binding, spin, isotopic, and thermal effects on scattering as well as to clarify instrumental problems such as multiple scattering in the samples.

How rapidly these questions were resolved is dramatically illustrated by the literature of 1948. In that year the first description of the techniques was given; the first applications to n-p scattering, hydrogen atom location, and alloy structures were described; and the first review article appeared.

In late 1948 and early 1949 there began a series of investigations on the scattering produced by substances whose atoms possess magnetic moments. The complete results of this work, together with results of continuing studies of nuclear scattering problems, appeared in three major papers, all published in 1951. (I joined the group in 1949, and Mike Wilkinson joined in 1950.)

In the first of these papers, the magnitudes and signs for nearly a hundred nuclides were reported; included were discussions of their implications to theoretical nuclear physics and structure determinations.

In the second paper, the Halpern–Johnson theory of paramagnetic scattering was verified, the magnetic form factor and radial moment distribution of Mn^{++} were measured, and the first direct evidence for an antiferromagnetic state was obtained. In the third, scattering from ferromagnets was systematically studied. Here the Schwinger form of the magnetic interaction of neutrons with atomic moments was verified with high precision. In the course of these experiments, the use of Bragg reflections from magnetized single crystals was developed for application to polarized neutron studies.

The powder diffraction technique had thus become a powerful, and in some cases unique, research tool. However, even more than in x-ray diffraction, the powder technique in neutron diffraction is inadequate for the study of complex crystal structures. In 1951, S. Peterson (now at Argonne) and Henri Levy investigated systematically the reflectivity of single crystals; they concluded that the estimates for maximum permissible crystal dimensions originally given by Bacon and Lowde were unduly pessimistic and that, in general, it was possible to find an acceptable compromise between crystal size and available intensity. With this investigation, neutron crystallography was launched. Because of the favorable scattering power of hydrogen for neutrons, emphasis has been centered on hydrogen-containing compounds. The first hydrogen-bonded compound to be studied by single-crystal technique was KHF_2, for which Peterson and Levy showed that the F—H—F bond is symmetrical with no detectable departure from spherical symmetry in the vibration of the proton. This investigation was also the first to determine Fourier projections of scattering density from neutron scattering data.

At each of the second-generation reactors developed between 1948 and 1958 (NRX in Canada, BEPO at Harwell, BGRR at Brookhaven, JEEP in Norway, MTR in Idaho, EL-2 at Saclay, and CP-5 at Argonne), strong and active groups working with neutron scattering developed. At Oak Ridge, the primary source of neutrons continued to be the now low-flux Graphite Reactor. Only toward the end of this period, with the commissioning of the ORNL Research Reactor (ORR) in 1958, did ORNL obtain a more intense neutron source. Because of this low flux, the experiments carried out by the group then in the Physics Division (Wollan, Shull, Koehler, Wilkinson, Cable, and Child) and that in the Chemistry Division (Levy, Peterson, Busing, and Smith) continued to be elastic scattering experiments in which the final momentum of the neutron is measured, but at the same energy as that of the neutrons incident upon the sample—crystal structure, magnetic structure, magnetic disorder in alloys, etc.

In 1955, at Chalk River, B. Brockhouse and his associates initiated their studies of inelastic neutron scattering. In such experiments the energies as well as the momenta of the scattered neutrons are measured. Brockhouse et al. devised the first triple-axis crystal spectrometer and invented the now commonly used constant Q (wave vector) and constant E (energy) methods of operating the instrument. Because the energies of neutrons having wavelengths that approximate interatomic spacings are comparable to the energies of excitations in solids (phonons, magnons, crystal field energy splittings, etc.), the energy gain or loss of the neutrons on scattering is readily measurable. Neutron inelastic scattering measurements can provide a wealth of information about the interatomic forces in solids as well as about the strength of magnetic exchange interactions, to cite just two examples. Such experiments require high incident intensity, however, and were not attempted at the Oak Ridge Graphite Reactor.

When the ORR came on line in 1958, it gave Oak Ridge a distinct, if brief, edge in neutron source strength. The ORR (and its sister reactor, the Materials Testing Reactor), having a flux of the order of 3×10^{14} neutrons cm^{-2} sec^{-1}, was then the world's most intense neutron source used primarily for research. The programs that used the Graphite Reactor were transferred to the ORR but with new and more elegant instrumentation. It was during this time that Levy and his group developed their automatic, four-circle diffractometer, and Wollan and his group developed the rotatable magnetic field diffractometer with which many of the exotic magnetic structures and structure transformations in the rare earth metals and alloys were determined.

In 1964, Wilkinson, who by then had moved to the Solid State Division, and Harold Smith, who had transferred into the same division from the Chemistry Division, set up the nucleus of a neutron spectrometry program and began construction of a triple-axis spectrometer at the ORR. They were subsequently joined by R. M. Nicklow and later by H. A. Mook. The first problem to be completed at this instrument was a study of the lattice dynamics of copper as a function of temperature, with special attention to anharmonic effects. Investigations of other more complicated or more difficult problems in lattice dynamics, such as are found in gallium and lithium, were started, but they were not completed because of lack of intensity in the neutron source. (They were later finished at the HFIR.)

Meanwhile the design and construction of the Oak Ridge High Flux Isotope Reactor (HFIR) was under way, and new flexible instrumentation for this reactor was designed. With the startup of the HFIR, ORNL once again had, and has to this day, the most intense neutron source for research in existence. The physics group, which had been joined by Ralph Moon, transferred into the Solid State Division. Ernie Wollan at this time was lost officially to retirement, but he continued (and still continues) to take an active interest in the research of the division.

At first, three of the four horizontal beam holes at the HFIR were instrumented. Of these, HB-3, which is a tangential beam hole, was equipped with a conventional triple-axis spectrometer of exceptionally rugged and precise construction. Under optimum conditions, the flux at the sample on this instrument is unsurpassed anywhere. At HB-1, an instrument unique in this country and duplicated only recently at the Institut Laue-Langevin was installed. This is a triple-axis, polarized-beam spectrometer, the analyzing crystal of which is polarization-sensitive. With this machine, the final momentum, final energy, and final spin state of the projectile neutrons are measured. This constitutes the maximum possible information about the target. The instrument at HB-2 was installed by the Crystal Chemistry Group, now expanded to include Carroll Johnson and George Brown. At HB-2, the high flux of the HFIR is exploited to permit crystal structure determinations at high resolution on complex organic compounds. Each of these three instruments is controlled by its own dedicated PDP-8 computer. The control programs evolved from those written by Busing and Levy for a computer-controlled, x-ray diffraction system, another first for ORNL.

The fourth beam port, HB-4, was equipped with a novel time-of-flight spectrometer. This is a device for doing neutron inelastic scattering experiments, in which the incident beam is pulsed and the time taken for the neutrons scattered by the sample to reach a detector is recorded. If the neutron gains energy in the process, it arrives in a shorter time than the elastically scattered neutron; if it loses energy, it takes longer to arrive. The chopping is done in this instrument by varying the direction of the net magnetic field on a monochromating ferrite crystal, a scheme which was suggested in a paper by Shull, Wollan, and Strauser in 1951. The duty cycle of the device may be made to approach 50% by pseudo random pulsing. To analyze the data from this correlation chopper, we must disentangle them from the pulsing sequence by means of a dedicated PDP-15 computer.

At the same time that the chopper was added, the triple-axis instrument first put into operation at the ORR was transferred to a side port of HB-4. Eventually, each of the other beam ports will be equipped with a satellite spectrometer.

The three research reactors built since 1965 are at present the world's only high-flux, steady-state reactors. The technology for steady-state reactors is probably near its limit. Dick Cheverton, who had much to do with the design of the 100-MW HFIR, believes that a super-HFIR running at 200 MW could be built and operated at a reasonable cost. To go beyond effective fluxes of 10^{16} neutrons cm^{-2} sec^{-1}, it is likely that we must come full circle and turn again to pulsed sources. Consideration is now being given to photo-neutron and spallation sources associated with electron linear accelerators and with proton cyclotrons. It is not unlikely that a low-power prototype of one or both of these instruments will come on line by about 1980.

Let me close this brief history with a short summary. The neutron scattering program at ORNL is one of the best research programs in the world engaged in obtaining fundamental microscopic information on condensed matter. This information is essential in understanding the physical properties of materials. These investigations are not only necessary to increase our knowledge of the solid state sciences, but also are extremely important in helping to solve the long-range energy requirements of our country. Almost every energy technology is materials-limited, and a better understanding of the physical properties of materials is necessary for the development and characterization of the new materials that will be required.

As we have seen, the application of neutron scattering techniques to investigations of condensed matter had its origin at ORNL in 1946 and has spread to almost every reactor center in the world. Throughout this 30-year period, ORNL has maintained its leadership in this very important research, although a strong challenge now exists from the Institut Laue-Langevin because of the excellent facilities and sound financial support that have been provided there. The ORNL program uses the HFIR, which provides the most intense thermal neutron beams now available for research, and the ORR, where facilities of a specialized nature have been developed to supplement the HFIR work and to extend the range of problems and materials that can be studied at ORNL. (It is important to recognize that the ORR is still the third most intense neutron source in the country.) The general areas of investigation include superconductivity, superfluidity, magnetism, interatomic forces in solids and liquids, defects in solids, chemical and magnetic crystallography, molecular structures of biological interest, structures of liquids, chemical and magnetic phase transitions, order–disorder phenomena in alloys, effects of atomic environment on physical properties, hydrogen bonding and diffusion, voids in irradiated materials, and high-conductivity organic compounds. The research is performed by staff members of the Solid State and Chemistry Divisions, and many cooperative programs exist with scientists from universities and other research laboratories.

We have come a long way since those early days on the third level at the Graphite Reactor. Fortunately, there is more to do and farther to go.

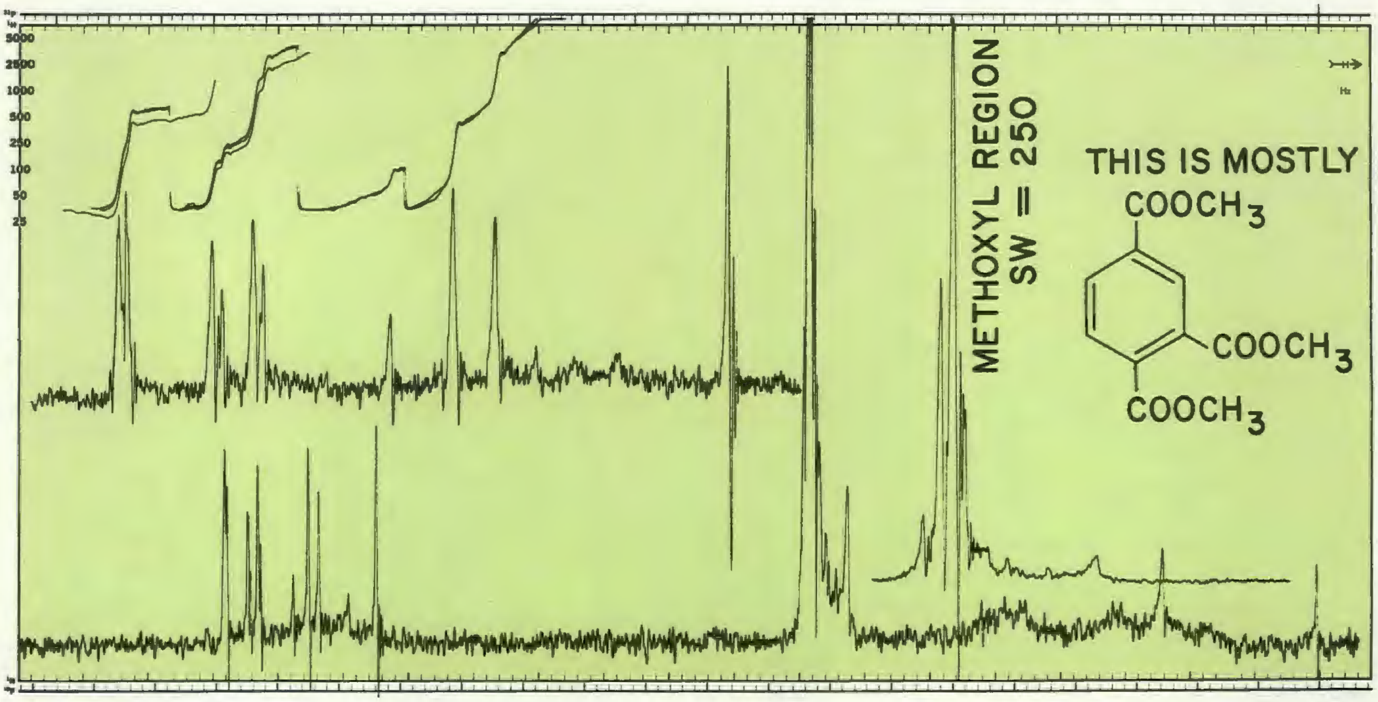
Ben Benjamin has been using NMR spectroscopy for his organic chemistry research since 1960. Up until two years ago, he did his research with small NMR units at the University of Tennessee and a 60-MHz unit at ORNL. Then, in early 1974, ORNL installed a new advanced 100-MHz unit just in time to help researchers getting involved with nonnuclear energy projects such as coal studies. Benjamin, who holds a Ph.D. in organic chemistry from the University of Florida, is responsible for the operation of the new NMR facility. Lloyd Brown operates the unit and assists researchers using the unit to analyze chemical substances. A chemist, Brown has worked in isotopes separation and has invented a process for separation of carbon-13. At right, Benjamin and Brown (sitting) inspect an rf transmitter, an electronic component of the NMR unit.

JIM RICHMOND

The NMR Detective

By CAROLYN KRAUSE

Suppose you have a sample of complex molecules containing hydrogen and you want to determine how many hydrogen atoms are in each molecule and what their relative positions are. Or suppose you simply want to know what the substance is. In either case, your best bet is to take the specimen to one of the most versatile detectives since Sherlock Holmes—ORNL's new advanced Nuclear Magnetic Resonance (NMR) Spectroscopy Laboratory in Building 4500N. The $200,000 facility is now capable of "fingerprinting" materials containing hydrogen and carbon-13; it could obtain NMR spectra for other elements if fitted with the appropriate



electronic components. Already, the two-year-old NMR facility has assisted ORNL researchers in determining the structure of some organic compounds derived from coal, studying the mechanisms of organic rearrangement reactions, ascertaining which characteristics of nitroso compounds fed to rats may be responsible for causing cancer in these experimental animals, and understanding the chemistry of molten salts.

The chief components of the NMR facility are a 38-cm, 3.6-tonne circular magnet having a field strength of 23,490 gauss; cabinets containing electronic components for transmitting and detecting radio frequency (rf) radiation; a sample holder or probe for spinning the specimen to be irradiated in the powerful magnetic field; and a computer to store and process data. Results are either plotted on a recorder as frequency spectra or presented in tabular form by the computer.

NMR is based on the principle that atoms having a nucleus with an odd mass number or charge will absorb electromagnetic radiation of a characteristic frequency and wavelength when placed in an external magnetic field. Like electrons, these nuclei have an angular momentum, or spin, which has associated with it a magnetic field, or magnetic moment.

According to Ben Benjamin, an organic chemist in the Chemistry Division who uses NMR spectroscopy extensively: "An assemblage of such nuclei will exist with equal numbers of all possible spin states, but, when placed in an external magnetic field, they will become oriented with the field with a slight excess of nuclei in the lower energy spin state. When irradiated at the appropriate rf frequency, some nuclei will absorb energy and 'flip' to a higher energy spin state. It is this absorption of energy that is detected and measured, giving rise to the NMR signal." The NMR signal, which appears on a recorder chart as a series of peaks, indicates the presence of certain nuclei.

Benjamin continues: "When the rf radiation is removed, some of the nuclei at higher energy spin states in the magnetic field will transfer their excess energy as heat to the surroundings, and the assemblage will return to its original spin distribution. This release of energy is known as the nuclear 'relaxation' process. Relaxation processes are important in determining the characteristics of the NMR signal and also are significant in the study of some chemical phenomena."

"Nuclei having a spin of ½ typically have long relaxation times and exhibit narrow, or high-resolution, NMR signals," Benjamin

This is an NMR spectrum of a sample derived from the controlled oxidation of coal, mostly the methyl ester of 1,2,4-benzene tricarboxylic acid. V. F. Raaen obtained the sample from a complex mixture of acids after methylation and separation on the gas chromatograph. The upper trace was taken at higher resolution, expanded scale, so that the peak separations can be measured. The histogram represents the number of hydrogens giving rise to the peaks.

explains. "Other nuclei with a spin greater than ½ possess an additional property, a quadrupole moment, which interacts with the magnetic moment, resulting in short relaxation times and very broad NMR signals."

"Fortunately," Benjamin says, "one of the most abundant elements in organic compounds, hydrogen, has a spin of ½ and a large magnetic moment, making it extremely useful for NMR studies. Hydrogen atoms at different positions in organic compounds are subject to slightly different internal magnetic environments because of the circulation of electrons; hence, they absorb rf energy at slightly different frequencies in a static external magnetic field. Thus, a methyl group (CH_3) will give a signal at a different place in the spectrum from a hydroxyl (OH) group. This property is known as the 'chemical shift.' It is also immediately apparent that the intensity of the methyl signal is three times that of the hydroxyl signal. The areas under the signal (shown as peaks on the recorder chart) are proportional to the number of hydrogens giving rise to the signal."

Hence, the varying intensities (areas) of the peaks in the spectrum indicate the number of hydrogen atoms in the complex molecules and their relative chemical shifts in relation to the position of the hydrogens in the molecule as well as the other kinds of atoms in the environment of the hydrogen. Some hydrogen NMR signals are quite complex; that is, they are split into a number of components. The appearance or complexity of the signal depends on the number of near neighboring hydrogens and their distribution in space. These splittings are a result of spin-spin interactions known as "coupling constants." By analyzing the three kinds of information in the spectrum (chemical shifts, intensities, and coupling constants), ORNL researchers can determine the structure and composition of chemical compounds.

The NMR facility at the Laboratory can also be used to study organic structure with carbon spectroscopy. However, the most abundant isotope of carbon (carbon-12) has an even mass number and charge and therefore no magnetic moment. On the other hand, carbon-13, which has a natural abundance of 1%, has a magnetic moment and a spin of ½. Natural abundance carbon-13 NMR spectroscopy has rapidly become an extremely important technique with the availability of sophisticated modern signal averaging equipment. Although carbon-13 NMR spectroscopy is more difficult and time-consuming than hydrogen NMR, the principles are nearly the same and many organic chemists believe the information is more rewarding.

Lloyd L. Brown, a chemist associated with the NMR facility says, "We can study the chemistry of appropriate samples at temperatures between —150 and 200°C. We prefer to operate with pure liquids or solutions of pure compounds, but we frequently find it possible to determine the composition of complex mixtures. Only very small samples are required; 10 mg of a sample whose molecular weight is about 200 is perfectly adequate, but it is possible to work with only micrograms by accumulating thousands of spectra in a short time (Fourier transform NMR spectroscopy). The NMR spectroscopy is nondestructive. The sample is not consumed, and after analysis, it is available for other types of measurements."

The first NMR experiments were carried out in 1946, and the first commercial NMR spectrometers were made available commercially in the mid-1950s. Small units are now used by universities for undergraduate teaching and research. Some universities have several advanced NMR units complete with sophisticated computers. Spectrometers are available for operation at 60, 80, 90, 100, and 220 megahertz (MHz), with the most advanced state-of-the-art units operating at 270, 300, and even 360 MHz. The ORNL facility operates at 100 MHz for hydrogen. Such a spectrometer is too expensive for many small universities; hence, the ORNL unit is used in the summer by a number of faculty members and students from various university programs.

Coal Research

The NMR facility is largely used by the Chemistry Division's group of organic chemists—Benjamin, Clair Collins, and Vernon Raaen. Raaen has been leading an effort in basic coal research in which NMR spectroscopy plays an important role. His work at present involves studying the structure and composition of products yielded by low-temperature partial oxidation of coal.

Raaen says that the procedure involves grinding up coal—specifically the vitrinite maceral of bituminous coal—and mixing the pulverized coal with diatomaceous earth (a natural silicate) to allow percolation of the oxidizing chemical. The powdery mixture is placed in a column through which the oxidizing agent, potassium permanganate in water, is passed. As a result of the oxidation process, potassium salts of acids are produced. The acids are then extracted by solvents and identified by NMR spectroscopy. The resulting information will be used in deducing the structure and composition of various organic compounds in coal.

"When I oxidize these compounds, I get ordinary molecules like acetic, propionic, butyric, oxalic, and benzoic acids as well as many acids having higher molecular weights," Raaen says. "But there are no detectable olefins (organic compounds with double or triple bonds)." Identification of various acids by NMR is further confirmed by other methods such as gas chromatography; but Raaen says that, without the availability of advanced NMR spectroscopy at ORNL, analysis of the organic chemical content of coal would be "extremely tedious."

What have ORNL's organic chemists learned from NMR spectroscopy about coal's hydrogen content (which is lower than that of petroleum) when looked at in terms of the ratio of hydrogen to carbon? "By integrating the areas under the peaks, we can determine the relative aliphatic to aromatic hydrogen content," Raaen says. "Also, NMR spectroscopy can give us the ratio of hydrogens on carbons bound to aromatic rings vs strictly aliphatic hydrogens." Aromatic compounds are nuclei of hydrogen and carbon linked together in single- or multiringed structures. Examples are benzene and naphthalene. Aliphatic compounds contain straight or branched chains made of carbon and hydrogen. Propane and butane are simple examples.

Raaen has found that the aromatic compounds in the coal he has analyzed contain one-third of the hydrogen while the aliphatic compounds contain the remaining two-thirds of the hydrogen. Breaking down this distribution further, Raaen has found that "half of the aliphatic hydrogens are on carbons directly bound to rings, and the other half are on carbon atoms more distant from the rings or chains."

Raaen observes that, when sufficient knowledge about the composition and structure of organic compounds in coal is gained, it will be of use to coal conversion technologists in selecting catalysts and processes to get the optimum yield of desired coal products.

To use NMR for chemical analysis of these coal derivatives, or of other organic substances, Raaen says that the compounds must be dissolved in solvents that are free from ordinary hydrogen. Because the best solvents contain hydrogen, Raaen has chosen solvents substituted with heavy hydrogen, or deuterium, which does not absorb in the same region of the NMR spectrum as do the samples under study. Among the solvents he uses are deuteropyridine, deuteroacetone, and deuterochloroform, all relatively expensive compounds.

Cancer Research

Several NMR users are from the Biology Division, which has supplied some of the funds to meet the capital and operating costs of the NMR facility. One group particularly interested in NMR studies includes Willie Lijinsky, biochemist, Wayne Taylor, veterinary pathologist, and George Singer, organic chemist. This group has been conducting biochemical studies in hopes of understanding the chain of events by which nitroso compounds fed to rats transform normal cells into cancer cells. The group has demonstrated that nitrosamines are formed in the stomachs of rats when they are fed amines and nitrites. Many nitrosamines have been found to be carcinogenic, causing cancers of the lung, liver, and esophagus in rats. Amines are present in foods, medicines, and environmental chemicals. Nitrites, formed by the bacterial reduction of nitrates, may get into the human stomach through the ingestion of plants grown in nitrate-fertilized soil, water high in

JIM RICHMOND

Vernon Raaen points out a peak in a coal spectrum on the recorder. Looking on are Benjamin and Brown, who is sitting at the operating console which controls the NMR spectrometer.

nitrate content, and sodium nitrite, which is added as a preservative and coloring agent to some meats.

Lijinsky's group has done several studies demonstrating that some nitroso compounds are more carcinogenic in rats than are others. For example, the group has found that carcinogenic activity decreases significantly when the hydrogen on the carbon atoms adjacent to the nitroso group is replaced by deuterium. Carcinogenic activity ceases almost completely when these hydrogen atoms are replaced by methyl groups. The group has hypothesized that the first step in changing normal cells into cancer cells in rats may occur when this hydrogen atom is removed from the nitroso compound, probably by reaction with an enzyme in the rats' bodies. Apparently, nitroso compounds containing deuterium instead of the alpha hydrogen are much less carcinogenic because the carbon-deuterium bond is stronger than the carbon-hydrogen bond; therefore, it is more difficult for the deuterium to be removed in reaction with the enzyme. In the case of methyl substitution, there is no hydrogen atom to be removed; hence, there is a loss of activity.

Singer is using the NMR facility to study (1) the rates at which hydrogen is removed from certain nitroso compounds dissolved in a chemical medium simulating rat enzymes and (2) the three-dimensional spatial geometry of the nitroso compounds to determine what relationship exists, if any, between the reactivity (cancer-causing activity) and conformation (shape) of the nitroso molecules. Singer says that the rates of removal of the hydrogen are of interest because of the hypothesis that nitroso compounds from which hydrogen can be removed fastest in enzyme reactions are the most carcinogenic and most reactive.

Singer already has conducted several studies using NMR to determine conformation of nitroso compounds such as nitroso morpholine and dimethyl nitrosamine, which is known to cause cancer in humans. He says that NMR spectroscopy is the "ideal tool" for studying shapes of organic molecules in three dimensions because it records the patterns of signals generated by all the hydrogen atoms in the molecules and because these patterns are uniquely characteristic of the chemical environment of each hydrogen.

To study the rates of removal of hydrogen from nitroso compounds, Singer dissolves the compounds in solvents containing deuterium and a base to simulate enzymes. He uses solvents such as deuterated methanol and sodium deuteroxide. In the deuterium-containing solvent, the nitroso compound's atoms are replaced by the deuterium in the solvent. This reaction can be followed by NMR spectroscopy, which detects a decrease in absorbed rf radiation as the hydrogen is removed and replaced by deuterium. The signal decreases as hydrogen is removed because the deuterium absorbs rf radiation at a frequency different from that at which the sample is being irradiated. The rate at which the signal decreases indicates the rate at which hydrogen is removed from the nitroso compound under study.

Molten Salt Studies

Jerry Braunstein and Tony Bacarella of the Chemistry Division have been using NMR spectroscopy to increase their understanding of the motions of charged and neutral constituents in concentrated aqueous electrolytes and molten salts. In particular, they have been measuring electrochemically the diffusion coefficients, or rates of movement, of cadmium cations dissolved in hydrous melts of calcium nitrate—$Ca(NO_3)_2 \times H_2O$—under different conditions, such as different temperatures and different concentrations of the calcium nitrate salt in water. During the past year, Braunstein and Bacarella used the NMR facility to study samples of hydrated calcium nitrate as a function of various temperatures and salt-to water ratios. The NMR facility detects hydrogen nuclei in the water molecules in this particular aqueous electrolyte. Braunstein and Bacarella found in preliminary studies that there is a strong correlation between the proton spin-lattice relaxation times and the diffusion coefficients for cadmium ions as the temperature and salt-to-water ratios of the hydrated calcium nitrate are varied. This suggests that the same transport mechanism that applies to the more massive ions may apply to the protons of the water molecules, as distinct from the situation in dilute aqueous electrolytes. Proton spin relaxation times refer to how long it takes for protons, after being saturated with rf energy in the magnetic field, to give up this energy to the surroundings, or lattice, and to return to their original spin orientations after the rf radiation is removed.

Braunstein says that they hope to use NMR spectroscopy to study the transport properties of other aqueous electrolytes and molten salts containing water. They also plan to use a device to be installed this year at the NMR facility to arrive at proton diffusion coefficients directly.

The understanding gained by Braunstein and Bacarella of the rates at which dissolved salts move through solutions may have applications in the development of energy sources. Braunstein says that better understanding of transport properties of aqueous electrolytes like potassium hydroxide could aid in improving the efficiencies of water electrolyzers and thermochemical cycles for producing hydrogen, which increasingly is in demand for fuel, coal liquefaction and gasification processes, and production of ammonia-based fertilizers. Electrolyzers decompose water into hydrogen and oxygen by passing an electric current between electrodes immersed in water to which an electrolyte is added. Thermochemical cycles make use of sequences of chemical reactions at different temperatures to accomplish the separation of water into its elements.

Another possible application of this knowledge of salt solutions is in the area of geothermal energy, Braunstein explains. Hot water rising to the surface from deep within the earth interacts with rocks and magma and leaches out salts. The water reaching the surface in some instances is a highly concentrated salt solution, which can foul steam generator systems that convert the heat energy of the water to electricity. An understanding of the rates of diffusion of salts through geothermal water may help in the development of methods to prevent dissolved salts from precipitating on the pipe walls in steam generators and causing corrosion and possible loss of heat transfer.

Other Research

"So far the NMR facility at ORNL has been used in the research of 33 staff members," Benjamin says. "We have looked at the proton spectra of some organic platinum complexes, identified the organic constituents of a process stream, and identified numerous previously unknown compounds. We have also studied the behavior of model protoplasm systems under freezing conditions and have determined the conformations of biologically important systems."

Benjamin has been working with Dave Doherty of the Biology Division on the spectra of some new polypeptides in hopes of finding a relationship between the structures and conformation of the peptides and their radiation protection activity as well as their enzyme inhibitor activity in leukemia victims. (Experiments on animals given peptides have shown that the chemicals make the animals more resistant to radiation damage and block the action of certain enzymes that allow the development of leukemia.)

"One of the most interesting ways of using NMR," Benjamin says, "is in the study of the course of molecular rearrangement. Some organic substances undergo reactions that produce a series of new substances having different structures in which the carbon skeleton has been scrambled.

"The typical experiment is rather complicated," Benjamin explains. "First, all or most of the new products must be separated and identified. Hydrogen NMR plays an important role in determining their structure. Second, many of the NMR signals must be assigned to individual hydrogens in the molecules. Next, it is necessary to synthesize the starting material containing an isotope (in this example, deuterium) in a specific, known, carefully chosen position. The isotopically substituted compound is reacted as before, and the products are again separated and examined by NMR spectroscopy.

"Because deuterium does not absorb in the hydrogen region, some signals may be missing or attenuated. With this information, it is possible to deduce how the products are formed, whether by hydrogen or carbon migration or by exchange with components of the reaction medium.

"In the past the group of organic chemists has spent most of its time on research of this type. Similar types of problems can also be solved by carbon-13 NMR either in natural abundance or enriched supply." NMR spectroscopy finds broad applications in all areas of chemistry and is indispensable to the modern organic chemist. It is valuable not only for determining structure and conformation but also for studying chemical equilibria and rate processes and in quantitative analysis. The NMR facility at the Laboratory is available to all ORNL scientists in need of this kind of information. Anyone doing research in which NMR might be helpful can bring his problem to Ben Benjamin for discussion.

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Just published is *Grants: How to Find Out about Them and What to Do Next*, by Virginia P. White, at one time executive assistant to the director of the Biology Division. Plenum Publishing Company, New York (1975). 354 pp. $19.50.

Awards and Appointments

In a recent competition held by the East Tennessee chapter of the Society for Technical Communication, a number of ORNL entries took prizes. Winner of the Francis McKinney Best of Show Award was the journal *Nuclear Safety*, edited by **W. B. Cottrell**, whose publication also won first place in the technical journal category. Cottrell also took first place in the technical news article category for "Plant Safety Features: The ECCS Rule-Making Hearing." Other winners: House Organ—"ORNL *Review*," **B. K. Lyon**, editor, first place; Bulletins—"International Conference on Heavy Ion Sources," **J. M. Asher**, editor, first place; Technical Reports—"An Assessment of the Environmental Impact of Alternative Energy Sources," **J. M. Asher**, editor first place; Bulletins—"International Conference on Fundamental Aspects of Radiation Damage in Metals," **W. E. Rodgers**, compositor, second place; Technical News Article—"ORMAK—The Oak Ridge Tokamak Controlled Thermonuclear Research Experiment," **A. D. Richardson**, designer, second place; Annual Reports—"Molten-Salt Reactor Program Semiannual Progress Report for Period Ending Feb. 28, 1975" (ORNL-5047), **G. W. Griffith**, editor, second place; Technical Reports—"FLANGE: A Computer Program for the Analysis of Flanged Joints with Ring-type Gaskets," **F. M. O'Hara** and **Sam E. Moore**, with E. C. Rodabaugh of Battelle, second place; Promotional Illustration, **Bonita Elmore**, first and second places; Industrial Photography, **John T. Maxwell**, first and second places; Pictorial Photography, **Charles Tucker** first and second places.

W. D. Shults has been appointed to the advisory board of *Analytical Chemistry*, a publication of the American Chemical Society.

Elected president-elect of the Health Physics Society beginning June 1976 is **J. A. Auxier**.

At the annual meeting of the American Nuclear Society in San Francisco last November, five ORNL scientists received the "Best Paper" award for 1973-1974 from the Society's reactor physics division. The honored authors were **G. de Saussure, E. G. Silver, R. B. Perez, R. W. Ingle,** and **H. Weaver,** who wrote "Measurements of the 238-U Capture Cross-Section for Incident Neutron Energies up to 100 keV," published in a 1973 issue of *Nuclear Science and Engineering*. The award included a $200 check, which the authors gave to Knoxville College. At the same meeting, **Betty Maskewitz** was cited for outstanding service to the ANS, its shielding and dosimetry division, and the radiation transport community worldwide.

Edward G. Struxness and **David E. Reichle** have been appointed associate directors of the Environmental Sciences Division.

John Martin has been elected a Fellow in the Institute of Electrical and Electronic Engineers (IEEE).

Elected chairman of the nuclear division of the American Ceramic Society for 1976–77 is **J. M. Leitnaker**.

Alex Zucker has been appointed member-at-large of the U.S. National Committee for the International Union of Pure and Applied Physics for a three-year term ending December 31, 1978.

James C. White has been appointed to the editorial advisory board of *Analytica Chimica Acta*, an international journal published in Amsterdam that is devoted to all branches of analytical chemistry.

Carroll Johnson has been elected vice-president of the American Crystallographic Association for 1976. This office, which is also that of president-elect, has been held previously by two other members of the ORNL structural chemistry group, W. R. Busing and H. A. Levy.

Early detection of lung cancer is a realistic goal to researchers like Paul Nettesheim, whose studies lately have centered on the effects of chemical carcinogens and radionuclides on the respiratory tracts of rodents. A native of Cologne, West Germany, Nettesheim received both an M.D. and Doctor of Medical Sciences (D.M.S.) degree in 1959 from the Medical School in Bonn. He also holds an M.S. in pathology from the University of Pennsylvania, where he has served as a pathology instructor. Nettesheim joined the staff of ORNL's Biology Division in 1963; six years later, he became group leader of the Respiratory Carcinogenesis Program. He also supervises studies of the biological effects of tobacco smoke, fossil fuels, and gaseous combustion products. Nettesheim is author or coauthor of more than 70 papers and is a lecturer at the University of Tennessee-Oak Ridge Graduate School of Biomedical Sciences. Here Nettesheim discusses scanning electron micrographs of healthy and affected epithelial tissue.

W. N. SHIPLEY

Early Detection of Lung Cancer

By PAUL NETTESHEIM

It is estimated that more than 80,000 Americans died from lung cancer in 1975, but the number is expected to be even higher in 1976. More than 80% of all diagnosed lung cancer cases die from the disease within a year after diagnosis. These facts may suffice to explain why lung cancer constitutes a major health problem deserving the commitment of considerable resources to improve means of its prevention and therapy.

To develop effective means of *prevention*, one must know the etiological agent(s), that is, the causative factor(s), of the disease. Among the man-made environmental contaminants deemed responsible for 80% of all lung cancers, tobacco smoke is the foremost candidate. There is strong evidence that other air contaminants, such as asbestos, radon daughters, bis-chloromethylether, chromates, and coke-oven effluents, also cause lung cancer in man at the high concentrations at


W. N. SHIPLEY

Rhonda Epler (l.) and Ann Marchok work at the incubator for epithelial tissue and the inverted-phase microscope.

which they are found in some occupational situations. In spite of our knowledge that these are the chief etiological agents, we have not succeeded in preventing the occurrence of tens of thousands of new cases every year, principally because not enough people are willing to avoid exposure, particularly to tobacco smoke.

The development of effective *therapy* for lung cancer has been similarly unsuccessful. Although surgical procedures, chemotherapy, and x-ray therapy, which are the main tools for cancer treatment, have become much more sophisticated in the last two decades, they have remained ineffective in the therapy of lung cancer. The reason for this is that in most cases the tumor has already reached an incurable stage by the time it is diagnosable with current procedures.

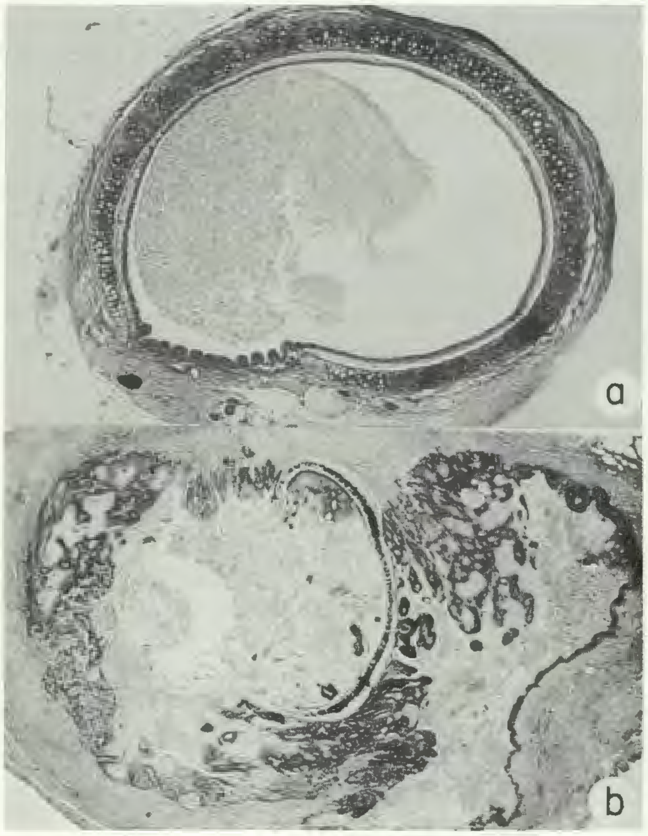
There is an obvious need to develop new approaches to the early *diagnosis* of lung cancer. This is not simply a matter of developing better instrumentation and hardware although much progress has been made in recent years in the refinement of bronchoscopy by the introduction of the flexible fiberoptic bronchoscope. Rather, to make significant advances in diagnosis, we must develop a better understanding of the *"evolution of cancer."*

Classically, the term cancer (or carcinoma, which is the term used for neoplasms, or abnormal new growths, derived from ectodermal tissues) has been used strictly to designate a tumor showing evidence of invasive and destructive growth. Without that evidence, most clinicians and pathologists have not been willing to make the diagnosis of cancer. This capacity to invade and metastasize to distant sites has been the cornerstone of the definition of cancer for centuries. Only recently have clinicians and researchers become aware of certain lesions that appear to precede invasive cancer. One of these is the "carcinoma in situ," also called intraepithelial carcinoma, which is a noninvasive stage of cancer. In short, it has become accepted that invasive cancer is only the fatal *end stage* of a disease process. The disorder apparently has multiple evolutionary phases, characterized by varying degrees of disturbance of cell and tissue growth and differentiation. Unfortunately, with the exception of carcinoma in situ, no "pre-neoplastic" lesions have yet been identified with any degree of certainty. It is well established, from human studies and animal experiments, that months and more often years elapse between the first (and perhaps only) contact with a carcinogen and the appearance of invasive cancer. However, little is known about the persisting cell and tissue damage during this so-called latency period. Various cell and tissue changes have been recognized in the respiratory tract epithelium of "healthy" smokers, but whether and how these are related to bronchogenic carcinoma is not known. Because bronchogenic carcinoma, once diagnosed, is virtually incurable, it is important to learn something about the existence and nature of the different pre-stages. The *precancerous* lesions or preneoplasias might be relatively easy to eradicate with the therapeutic tools now available. Because experimentation with humans is possible only in a very limited way, studies on laboratory animals must serve to close the gaps in our knowledge of the evolutionary process of bronchogenic carcinoma.

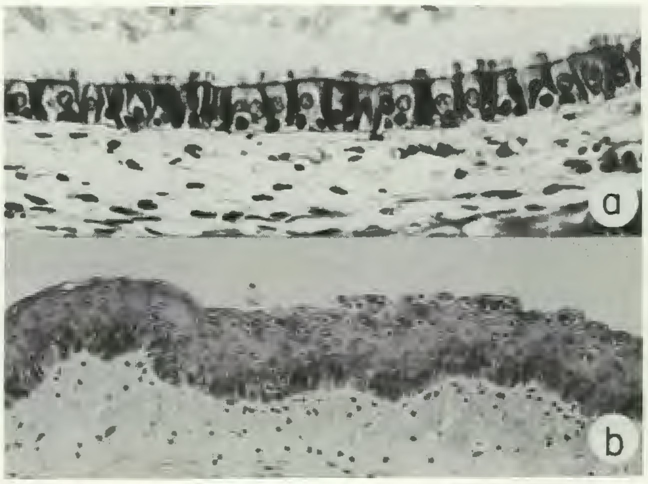
Investigations of the development of neoplasias and the search for and characterization of preneoplasias in the epithelium of the respiratory tract have become major focal points in the respiratory carcinogenesis group of the Biology Division in recent years. Some of the questions we are asking are:

1. Do some cell populations have a higher probability than others of becoming cancer cells?
2. If such preneoplastic cell populations occur, what are their morphological, biochemical, or functional characteristics? Can they be recognized, perhaps, with cell and tissue markers and distinguished from (*a*) "normal" cells of the same origin, (*b*) cells altered by toxic, but noncarcinogenic, agents, or (*c*) cells that are fully neoplastic?
3. If there is indeed an evolutionary series of preneoplastic lesions, can some of these lesions regress and disappear, as epidemiological studies on ex-smokers seem to suggest? How can we identify those lesions that tend to progress to cancer even after carcinogen exposure has ceased? What are the crucial factors that affect such regression or progression?

To even begin to pursue some of these questions, it was necessary to develop new experimental models that would allow us to expose preselected segments of respiratory tract to known quantities of carcinogen for predetermined lengths of time to produce cell populations with known "exposure history" and to subject them to various types of study and analyses. From studies in our own and other laboratories, we know that carcinomas resembling bronchogenic carcinomas in man can be induced in the respiratory tracts of rats and hamsters. For this, the animals are exposed to chemical carcinogens and radionuclides by either inhalation or intratracheal injection. What is not possible, however, with this approach—because of the anatomical and physiological complexities—is exposure to carcinogens (with the necessary control of dose and exposure duration) of a preselected target site within the organ system. Thus we cannot predict when and where preneoplastic lesions will appear. We therefore developed a method by which two or more standard-size pieces of rodent tracheas are grafted subcutaneously to the back of an isogenic recipient, a technique I devised with Don Martin, Dick Griesemer, and Joe Kendrick. The rodent trachea is anatomically and histologically very similar to the human bronchus. After these grafts are established, we insert cylindrical pellets containing a known quantity of carcinogen; the carcinogen is



Subcutaneous tracheal transplants in rats: (a) *Cross section through normal transplant containing mucus;* (b) *cross section through transplant exposed to carcinogen for several months. An invasive squamous cell carcinoma is destroying the transplant and infiltrating the surrounding host tissue.*



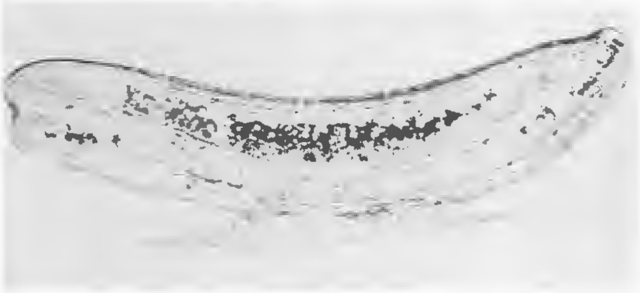
Epithelium of tracheal transplant: (a) *Normal transplants show a single row of ciliated and mucus-producing cells;* (b) *carcinogen-exposed transplants (7 days) show an early change in tissue differentiation called squamous metaplasia. The epithelium is 5- to 8-cell-layers thick.*

released from these pellets over days or weeks depending upon amount and concentration. The carcinogen exposure can be terminated at will by removing the pellets, whereupon the dose delivered to the target tissue is calculated from the amount remaining in the pellet. In this way we can expose tracheal epithelium to a known quantity of carcinogen over a given period of time and examine it either at the time the exposure is terminated or at any desired interval thereafter.

Using this system, we performed a number of investigations to determine the carcinogen dose range that would induce carcinomas and to elucidate the sequence of morphological events as a function of time of exposure to carcinogen. We found that, with 1 mg of benzo(a)pyrene, squamous cell carcinomas could be induced within 8 to 10 months in nearly all the animals. In contrast, earlier experimental models required anywhere from 30 to 50 mg of benzo(a)pyrene, given over 2 to 3 months, to induce a high incidence of lung cancers. We also found that, by using 7,12-dimethyl(a)benzanthracene, another carcinogenic aromatic polycyclic hydrocarbon, only 100 μg were required.

In addition we discovered that, within a few days after the start of carcinogen exposure, histologically recognizable changes of the tracheal epithelium occurred which resembled various lesions described in the respiratory system of humans, particularly heavy smokers and uranium miners.

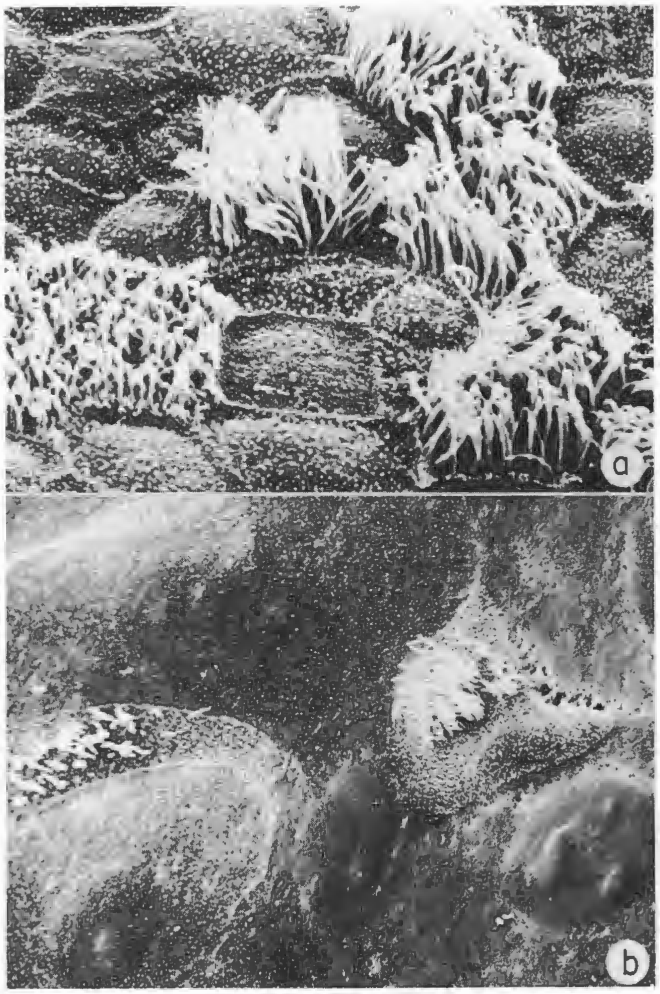
These findings demonstrated that the experimental model was indeed suited to our purposes. Next we needed to develop a means by which to study such altered respiratory-tract epithelium in greater detail, to make it accessible to frequent observation to examine its growth characteristics under various conditions, and to isolate cell populations so as to subject them to more detailed analysis. For this purpose, Ann Marchok devised an in vitro culture system to make it possible to maintain pieces of tracheal tissue for weeks and even months so that living tissue could be observed under the microscope and so that its rate of growth and state of differentiation could be mainpulated via various additives (such as nutrients and hormones) to the culture medium.



Tracheal organ culture that has been maintained in vitro for several weeks. Under the proper culture conditions, epithelial cells (top layer) will migrate over the edge of the explant onto the culture dish (bottom).

We found that such organ cultures remained responsive to physiological stimuli and that it was possible not only to stimulate mucus production by adding vitamin A to the medium but also to change the mucociliary epithelium to a squamous epithelium producing keratin instead of mucus by withdrawing serum as well as vitamin A. Such a change in epithelial differentiation occurs in humans and animals alike under conditions of vitamin A deficiency. Further studies showed that addition of small amounts of two hormones, insulin and hydrocortisone, markedly stimulated the formation of cell products such as mucus or keratin, depending on the state of differentiation. Subsequently, culture conditions were established in which the epithelial cells migrated from the organ culture onto the culture dish. In such "outgrowths," the epithelial cells leave the original tissue boundaries and grow without the normally supportive submucosal connective tissues, cartilage, etc. By use of the enzyme trypsin it was possible to rid the epithelial cell populations of fibroblasts, thus establishing primary cultures of pure respiratory-tract epithelium.

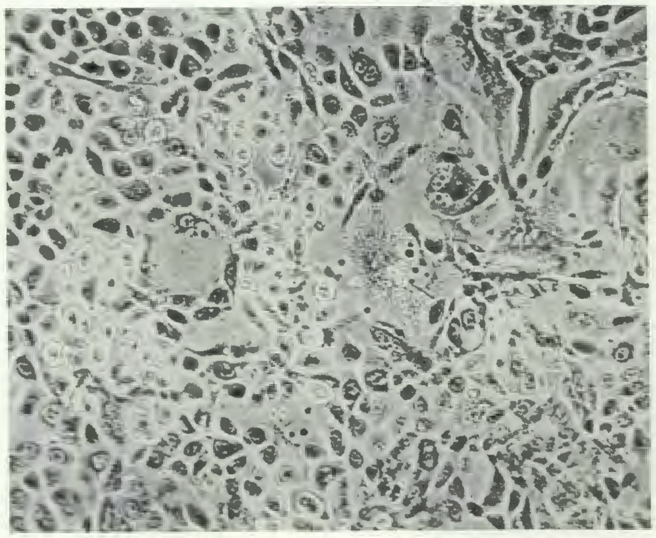
With these in vivo and in vitro systems at hand, we were now able to expose respiratory-tract epithelium under in vivo conditions to carcinogen and to study the resulting cell and tissue changes both in vivo and in vitro. In one type of study, we examined the fate of epithelial lesions induced in vivo by different amounts of carcinogen when the exposure was short—14 days. At the dose levels tested, tumors were not expected to develop before 9 months to a year. Carcinogen-containing pellets were inserted into the lumen of established tracheal grafts carried under the back skin of inbred rats. Two weeks later, the pellets were removed. Some tracheal grafts were processed for histological study and others were left intact in the animals to be sampled at later time intervals. We hoped to learn whether the epithelial changes that were observed at the end of this short exposure interval, namely massive and widespread squamous metaplasia with varying degrees of keratinization, would (1) regress after exposure was stopped; (2) progress to lesions that might be recognized as precursors of cancer, and eventually to cancer; or (3) remain stationary, that is, unchanged for a long period of time.



Scanning electron microscopy of tracheal organ cultures and cell cultures: (a) *Several cells with long cilia and nonciliated cells with numerous microvilli are recognizable in this photograph of an established tracheal organ culture;* (b) *epithelial cell cultures derived from cells migrating from the organ culture piece also show ciliated and nonciliated cells.*

The term "squamous metaplasia" denotes a change of the normally mucociliary epithelium of

Permanent epithelial cell line derived from a tracheal organ culture preexposed to carcinogen in vivo. The dramatically increased in vitro growth capacity distinguishes this cell population from normal epithelial cells. (Phase contrast photograph of a living culture.)



the trachea and bronchi to a skinlike epithelium that produces keratin instead of mucus. Such change in tissue differentiation has not only been described, as mentioned above, in cases of vitamin A deficiency, but also in humans known to be exposed to such carcinogenic contaminants of the breathing air as tobacco smoke. Some of these metaplastic changes have been thought of as precursors of neoplasia, particularly when associated with so-called nuclear atypias such as alterations in size, shape, and chromatin distribution of the cell nucleus.

We found that in almost all cases the abnormal, metaplastic epithelium disappeared within about two weeks following cessation of carcinogen exposure. By the end of two months, much of the epithelium had returned to normal, and only occasional tiny foci of metaplasia or other epithelial abnormalities persisted. It seems, therefore, that the severe early metaplastic alteration of the carcinogen-exposed epithelium is a response to the *toxic* rather than the tumorigenic properties of the carcinogen. This response disappears rapidly after termination of the stimulus, leaving little recognizable damage behind.

In the same study, some of the tracheal epithelium had also been placed into culture at the same time that the carcinogen exposure was terminated. For comparison, tissues not preexposed to carcinogen were maintained under the same culture conditions. This normal epithelium, although very stable, had only a very limited in vitro growth capacity. The rate of proliferation was low, and cells migrated onto the culture dish slowly. Such "normal outgrowths" had only a limited survival capacity, particularly after the tissue fragment from which they emanated was removed from the culture. In marked contrast, the epithelial cells from carcinogen-exposed tracheas grew rapidly in vitro, forming large epithelial outgrowths within a few days. These outgrowths, which could readily be subcultured, gave rise to a number of permanent cell lines. Transplantation studies with some of these cultures, however, showed that these cells are not (or not yet) neoplastic. These experiments clearly demonstrate that, following a brief carcinogen exposure in vivo, cells exist which, although they may not be recognizable morphologically, can be recognized because of their drastically altered growth characteristics in vitro. So far these cells cannot be detected by any other means because the early in vivo cell and tissue changes that are observed microscopically are of only transient nature and are therefore most likely not related to the carcinogenesis process. We suspect that the abnormal cells that can be detected by the in vitro test are the forerunners of cancer cells that have perhaps acquired some, but not yet all, of the growth characteristics of cancer cells. Obviously, these findings have raised many questions that need answering before any final conclusions can be drawn.

We are confident that this new approach will enable us to investigate the *early events in the evolution of neoplasia* so that we may learn to recognize cells that are on the way to becoming cancerous and find means to prevent the progression from premalignancy to malignancy.

Joy Rhoton works at the sterile hood used for tissue culture.

W. N. SHIPLEY

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Letter to the editor:

Steve Dean, m.c. on the T.V. talk show with Carol Utley, interviewing ORNL heads today, expressed surprise at the programs being carried out at ORNL and asked to be informed of more. I know of no better way than to send them copies of the Review.

I must compliment you and your staff for your presentation of scientific facts and information that even I, as a lay person, can understand. The layouts promote interest also. In fact, it's excellent.

I suggest that the Spring '75 issue be sent in particular to Mr. Dean in connection with his interest in TVA's steam plants.

Sincerely,

Mrs. J. Prislinger
Swafford Road
Concord, Tennessee

February 27, 1976

OAK RIDGE NATIONAL LABORATORY *REVIEW*
P. O. BOX X: OAK RIDGE, TENNESSEE 37830

E. O. Wollan and C. G. Shull set up a sample on the second diffractometer installed at the Graphite Reactor. The basic design of this instrument has been reproduced, on a larger scale, in laboratories the world over.