Oak Ridge Remembered: 1944-1949

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The purchase requisition read "one goat, one large-size Erector set, and one gross of condoms." Paul Tompkins chuckled as he told about the first requisition placed through the University of Chicago by its newly formed "Metallurgical Laboratory" in 1943. Paul merely wanted to study the radiation effects of uranium fission products in animals (the goat), and needed to design and build mechanical hands (the Erector set) with which to manipulate highly radioactive samples behind barriers. The group also needed some type of holder with minimum wall thickness (the condoms) for their dosimeters.

Waldo Cohn, Paul Tompkins, Ed Tompkins and other biologists had moved from Chicago to "Dogpatch" (as Oak Ridge was nicknamed) in 1944 when the Manhattan District Project opened the Clinton Laboratories. The mission of its inmates was to produce millicurie amounts of plutonium, and to study radioactive materials and effects of radiation in animals and people. This group was busily engaged in the study of fission products when I arrived at the Clinton Laboratories some months later.

The purpose of this essay is to fill in some of the gaps in the story of the transition of radionuclides from a laboratory curiosity to today's widely used tools. Although nuclear medicine as we know it was being practiced before World War II in Berkeley and Boston, it was the Manhattan Project that made its extraordinary growth possible. Little documentation exists for the events that occurred during and immediately after the Project days, and most of it is buried in Project literature. Although I will try to point out some of these events based on personal recollections, my pilgrimage began some distance from the established radioactivity centers.

In graduate school I was interested in color chemistry, but by dint of some persuasion, I was able to enroll in courses dealing with spectroscopy, atomic and molecular physics, and quantum mechanics. After graduation and teaching in Louisiana for 2 years, my listing in the National Roster of Scientific and Technical Personnel resulted in a telephone call from the War Department in 1944. I accepted a job, vaguely described as located "south of the Mason-Dixon line and east of the Mississippi," and was sent first to the Navy Yard in Philadelphia to work on a little-known (even today) project designed to separate uranium isotopes by thermal diffusion.

I had been in Philadelphia only a few days when a pivotal accident occurred. A tank containing 600 pounds of uranium hexafluoride had inadvertently been overloaded and blew up, killing two colleagues instantly and sparing me only because I happened to be standing in just the right place behind an armorplate shield, with some of the blast going below me and some over my head. The explosion wrecked the Philadelphia pilot plant beyond repair, and I was sent to Oak Ridge, where a full-scale thermal–diffusion plant was being built. We all worked prodigiously to get it completed, and it was in operation within 90 days.

Some months later it became clear that gaseous diffusion would win out as the method of choice for the separation of uranium isotopes, and that our thermal plant would be shut down. But my training in spectroscopic chemistry and other subjects related to nuclear physics, brought about my transfer to Waldo Cohn's group at Clinton Laboratories (now

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Oak Ridge National Laboratory), where biologists and others were working on the effects of radiation in animals and people, an exciting research program.

Among other things, Cohn's group was responsible for making radionuclides (called isotopes in those days), and shipping them to other branches of the Manhattan Project—Los Alamos, Chicago, Berkeley, etc. This was because the cyclotrons had been side-tracked into war-connected research, and there was an urgent need to use Oak Ridge's reactor to produce radioactive sources for medical and research purposes. Before the war, Aebersold, Seaborg, and others had used the cyclotron at Berkeley for the production of radioactive nuclides for use in experiments of various kinds, and some of the new materials had been passed along to Hamilton, Low-Beer, Lawrence, and others for research use at the medical school at Berkeley. In addition to conducting tracer experiments, this group had begun administering radionuclides (mainly P-32) to patients who had polycythemia vera, leukemia, or some other blood cancer. Since it was important to continue treatment of these patients after the cyclotron went to war, my first assignment was to prepare a curie of radiophosphorus for the Berkeley patients. In one of the ironies of the times, a news story in the Knoxville papers described how a 3-year-old child was being flown from Knoxville to Berkeley to get the new radioactive treatment for leukemia. During the previous week we had sent out the needed P-32 from Oak Ridge—only 20 miles from Knoxville.

When I started work at the laboratories, Waldo Cohn, Paul Tompkins, Ed Boyd, and others were busily studying fission-product mixtures. Ion exchange, solvent extraction, and, later, chelating agents all played significant roles in sorting out the dozens of chemically similar isotopes in these mixtures. Rather than try to catch up with the knowledge and experience that this group had amassed, I elected to study the use of the nuclear reactor as a chemical device and as a source of radioactive materials for use by physicians and for use in many kinds of research (*1–3*).

The first task in such a venture was to determine what could be produced in the reactor and in what quantities. This meant learning what was known about the effectiveness of slow neutrons in producing nuclear reactions. There was little information on the two most important parameters in this problem: the cross section (or reaction probability) for neutron capture and the numbers of neutrons available in the various parts of the "pile" as the reactor was then called.

Our first task was to measure the intensity of the neutron flux (neutrons/sq. cm/sec) along the length of the sample holder when it was inserted into the reactor (*4*). We set about measuring the amount of radioactivity produced in a given amount of a substance with a known neutron-capture probability. From this information we could calculate the neutron flux at the location under study. Knowing the neutron flux, we could then determine the cross sections for other materials by activating them at the same location and measuring the amount of radioactivity produced.

Short irradiation times could be used when the newborn nuclides were short-lived, but this often caused practical problems. I have vivid recollections of seeing Larry Glendenin put a sample in the reactor, leave it there for a few minutes, then take it out and race 100 yards down the hill to his laboratory. There, in desperate haste, he would transfer his sample and distill the "daughter" away from its "parent." With luck, he might still be able to identify and measure a daughter with a half-life of no more than a minute.

Two radionuclides whose production cross sections were well known were 2.5-hr manganese-56 and 5.3-year cobalt-60. Cross sections for their production were high enough so that good product yields were available (*3,5*). With the help of the metallurgy department, we devised an alloy of manganese and cobalt in such proportions that we could use the foil to monitor both short- and long-lived materials. By including a strip of the foil in the irradiation vessel, we could measure the Mn-56 activity with a short irradiation and the Co-60 activity if the bombardment was prolonged. It was frequently possible to measure more than one radionuclide in a sample by permitting the shorter-lived activity to decay and then measuring the residual longer-lived material. It was usually possible to locate samples of reasonably pure materials for these studies, often in the oxide form with no competing radioactivity. We were thus able to determine the yields for a large variety of radioactive substances.

Of course, methods for the reliable measurement of radioactivity became of paramount importance since it was necessary to make "absolute" measurements—namely determinations of actual disintegration rates, not just the counting rates. This led to two rather different types of problems since beta and gamma radiations behave quite differently. In late 1945 and early 1946 we tackled these problems with an expanded group, including Herb Clark, John Jones, Lloyd Zumwalt, and others. A well-type ion chamber was calibrated for gamma measurements (*6*); we worked on beta-particle behavior, studying backscattering, self-absorption, counting geometry, and so on (*7*). As we probed further into these

areas, it became apparent that we would be unable to perform many absolute measurements unless we knew the decay schemes of the radionuclides, i.e., the quantities and energies of the betas and gammas given off during disintegration. Since absorption curves for gamma photons were grossly inadequate, Wendell Peacock joined us to set up a thin-lens magnetic radiation spectrometer. Our team was eventually able to publish an atlas of the radionuclides that could be produced readily in the reactor. This atlas (*8*) contained decay curves, beta and gamma absorption curves, and yield calculations, for all of Oak Ridge's reactor-derived nuclides with half-lives greater than 12 hr.

With this set of tools, crude as they were by today's standards, we were able to develop a considerable body of information on the production of radionuclides. Then another idea surfaced: that of inverting the yield calculations and techniques to perform an elemental analysis. In 1937 Glenn Seaborg and others had used the cyclotron in this way to estimate the amount of gallium in meteorites by measuring the radioactivity produced by bombardment. From this quantity, they calculated the amount of gallium that must have been present in the sample. We used the reactor, with its tremendous neutron flux of around 500 billion neutrons/sq cm/sec, and found that the same type of analysis could be performed with much greater precision and sensitivity.

A sample containing an unknown quantity of an element could be irradiated along with a neutron-flux monitor. The resulting radioactivity was then measured, both in the monitor and in the sample under study. The desired radioactive component could be separated, either chemically or by its radiation characteristics, and its activity then measured. By knowing the flux value and using the previously determined cross section, a straight-forward calculation could be made as to the amount of the target element in the original sample. In this way we were able to determine minute quantities in the parts per billion range. Clark and I called this method "activation analysis" and introduced the term into the literature (*9,10*).

A plethora of other problems had to be solved during this period. Even during the war, a group of us had drafted a memorandum that listed well over 100 ways in which we thought radioactive materials could be used for peacetime purposes. We knew we could make large quantities of these nuclides, and we believed that they could be made inexpensively, at least compared with cyclotron production. But this meant that we must have ways of distributing them safely to people who needed them. It also meant that some type of organization was needed to assume responsibility for convincing the military establishment that radionuclides could be distributed to physicians, scientists, and industrialists with no threat to national security or to health. It was at this point that Paul Aebersold arrived on the scene to head the Isotopes Division of the Project and later of the Atomic Energy Commission. It was his job to set up the organizational machinery, not only to permit but also to encourage the distribution of the materials that we believed had such great potential.

But there were still technical problems to attack. What kind of shipping container should be used to transport the materials to distant places at a low cost? Lead was the material of choice for shielding gamma emitters but distance also attenuates radiation effectively, and can be used to reduce the needed amount of lead, and thus the weight of the shipping containers. With these parameters in mind, Mike Hawkins devised a container that both shielded the "hot" material and prevented a handler's hands and body from coming close to it. During irradiation the sample was contained in a 3-in. $\times$ ¾-in. aluminum can with a crimp top. A special can opener was devised, since the recipient must be able to remove the sample easily so as to minimize his own radiation exposure. Hawkins was also the designer of the radiation-warning symbol whose three-bladed propeller is still in use today.

One other problem from the early period might be mentioned. That was the ever-present question, "What charge should be made for the radioactive material?" It was agreed that no one should be permitted to make a profit from a project developed with government money, but if one tries to calculate real costs, how does one amortize institutions like the Manhattan Project? These discussions went on for many months, and a variety of costing approaches were tried. Finally, for want of anything more practical, we settled for a flat-rate charge per shipment.

Comparisons may be odious, but we did have occasion to discuss the cost and availability of cyclotron-produced phosphorus-32. To produce 1 Ci of radiophosphorus would require 8 days of cyclotron running time, at a cost of $15,000. At Oak Ridge we were offering radiophosphorus at a cost of $32.50 per curie. Our reactor could produce curies—and indeed kilocuries—of certain materials for the nation, and we could distribute them, for an essentially negligible charge.

But to return to Paul Aebersold's administrative problems. The military project management had real reservations about the advisability of making radionuclides available, even after the Smyth report gave away the "secret" of the atomic bomb. It was also

clear that some agency—presumably an academically oriented one—was needed to remove peacetime technology from its military heritage and give it to the world. William Pollard, then at the University of Tennessee in Knoxville, had caught a glimpse of this opportunity and was engaged in forming the Oak Ridge Institute of Nuclear Studies. This was initially a consortium of 12 universities, which later expanded to 45 members and assumed the name Oak Ridge Associated Universities.

In order to facilitate the release of restricted technology, Pollard and McDaniel of the AEC had long meetings in one or the other's office concluding with the preparation of a letter requesting information. They would then compose the reply, and Pollard would post his letter in Oak Ridge, while McDaniel would take the reply back to his office in Washington for mailing. Thus the establishment's log jam was broken.

Finally the various lines of research and development at the Laboratories converged with the administrative processes. The first announcement of the availability of radionuclides for peacetime uses was made by Waldo Cohn and his group in the June 17, 1946 issue of *Science*. Included in this paper was the list of all the fission products that could be produced and separated relatively easily, along with our lists of reactor-produced nuclides. When the first radioisotope shipment was made, on August 2, 1946, a full-scale press spectacle was staged, and the first public coverage of the reactor took place. The first shipments of radioactive material went to the Barnard Free Skin and Cancer Hospital in St. Louis and the Southern Research Institute in Birmingham, Alabama. Both were shipments of carbon-14, and were used for cancer research.

The production and distribution business flourished during the remainder of 1946 and through 1947, but a new problem soon loomed on the horizon. It became apparent that we could *make* most of the radioactive nuclides that were needed, but it also became apparent that there were not enough physicians and scientists trained to *use* radioactive materials safely and to interpret the results of their measurements correctly. Consequently, late in 1947 I discussed with Dr. Pollard the possibility of organizing a short-term training course for workers who were already skilled in their fields and who could put the radionuclides to work. Within two months, after Pollard, Aebersold, and Charles Dunham had exchanged the appropriate letters, the newly formed Atomic Energy Commission decided that the short-course approach was feasible (*12*).

Accordingly, in February 1948 I was asked to take leave of absence from the newly renamed Oak Ridge National Laboratory to organize three short radioactivity courses to be given during the summer of 1948. The plan for this first series of courses was to give training to selected university personnel, including medical school faculty, during the summer. Following this, the universities were expected to take over radionuclide training for the rest of the country. Staff from three university clusters in Texas, North Carolina, and the Washington–Oregon area were selected as cadres. Renovation of a building in downtown Oak Ridge was started in February 1948, and laboratory and detection equipment for 32 participants was purchased. Recruitment of a staff for the summer was begun, and the curriculum and experiments were designed between March and June, 1948.

The first course started in June, although admittedly the laboratories were not entirely completed when that class arrived. Meanwhile, announcements had been made to the medical and academic community, inviting applicants to fill the rest of the spaces available during the summer courses. The plan was to offer the three courses during the summer of 1948, after which I would return to ORNL. In the first few weeks, we received over 100 applications, including a large number from industrial firms who saw radioactivity as a means to attack some of their pressing problems. As a result, a fourth course was scheduled for October 1948 and we were submerged in the business of radioisotope training. An additional 100 applications were received during the fall, and it was decided to continue the courses into 1949.

Faculty for the first courses included Herbert Clark, Cyril Comar, Raymond Finkle, and Henry Lanz, all of whom contributed greatly to getting the program off the ground. About a third of the first 100 participants were from medicine, one-third from biology or related disciplines, and the remainder from the physical sciences and engineering. Incidentally, during the first 20 years of the Oak Ridge radionuclide training courses, well over 6000 participants were enrolled, with almost the same disciplinary distribution.

The foregoing has been a personal narrative designed to call to mind a few of the significant (or not so significant) events leading to the establishment of nuclear medicine during World War II and immediately thereafter. It might also be instructive to look at the state of the nuclear medicine literature during this period. Although there were isolated papers published in other journals, *Science* was the medium of choice for most of the official announcements regarding the radionuclide program. Tables 1 and 2 show a tabulation of papers in this field that

TABLE 1. NUCLEAR MEDICINE PUBLICATIONS IN *SCIENCE*, 1946–1949

Distribution by Field								
Year	1946		1947		1948		1949	
Volume No.	103	104	105	106	107	108	109	110
General	2	5	6	10	7	6	8	10
Basic science	1		3		9	4	2	2
Biology/ agriculture			1		3	1	7	5
Dentistry				1				
Biochemistry				1	4	2	4	3
Medicine								
Brain					1			
Bone						1	1	
Cardiology						1	1	
Thyroid						1		4
Liver						1		
Kidney						1		
Cancer								1
Total	3	5	10	12	24	18	23	25

TABLE 2. NUCLEAR MEDICINE PUBLICATIONS IN *SCIENCE*, 1946–1949

Distribution by Nuclide								
Year	1946		1947		1948		1949	
Volume No.	103	104	105	106	107	108	109	110
C-14			5	1	7	2	3	5
Deuterium			1					
I-131				2	2	1	2	7
Co-60					1		1	
P-32					4	1	1	5
S-35					2			
Ca-45						1	4	1
H-3						1		
Fe-59						1		
Mo-93 and Mo-99						1		
Na-24						1		
Hg-203 and Hg-205							1	
Sr-90								1

were published in *Science* between 1944 and 1949. Included are the numbers and types of nuclear entries by field and by nuclide. Beginning with the announcement of the availability of radioactive materials in June of 1946, the tables show a small but steady growth of publications in the use of various radionuclides during the ensuing three years, expanding from eight papers in 1946 to 50 in 1949. Comparison of this publication level with the present *Journal of Nuclear Medicine* may serve to dramatize the overall growth of nuclear medicine information, although even this comparison leaves out the many papers published in other journals.

It was an eventful 5 years, to be sure. We can add, with some satisfaction, that the only current use of radionuclides that was not included, in principle, in the wartime list of potential uses, is radioimmunoassay.

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* Dates shown for government reports are dates of declassification.