In Their Own Words:

Lathrop and Harper Recall Their Pioneering Work

In September 1994, the Department of Energy (DOE) Office of Human Radiation Experiments, in collaboration with the Lawrence Berkeley Laboratory, launched an oral history project. Historians traveled around the country to interview researchers and others with firsthand knowledge of human radiation experimentation during World War II and the Cold War. The interviewers sought to enrich the documentary record, elicit missing information, and provide researchers with a venue in which to share their thoughts on their activities. On January 26, 1995, Katherine A. Lathrop and Dr. Paul V. Harper were interviewed by Dr. Darrell Fisher from Pacific Northwest Laboratory and Michael Yuffee from the DOE Office of Human Radiation Experiments. A small sampling of excerpts pertaining to Lathrop and Harper's more than 4-decade scientific partnership and their seminal contributions in nuclear medicine is included here. The interview captures the rhythms of their collaboration: he more talkative and quick to move on to a new topic, she more precise and quietly filling in facts, each of them finishing the other's sentences and thoughts. They were frank about the ways in which early radiation research—largely unregulated and performed "on the fly"—differed from today's clinical trials and basic research. The full—and fascinating—text of the interviews is available at www.eh.doe.gov/ohre/roadmap/histories/0472/0472toc.html.

Selenium Tumor-Imaging Studies (Early 1970s)

YUFFEE: I don't think we've talked about metabolism studies with the selenium.

HARPER: (to Lathrop) Okay, selenium, that's your department, Katherine.

LATHROP: What do you want to know about selenium?

FISHER: Well, first of all, what were the events—

HARPER: Mrs. Lathrop spent some years in the Poisonous Plant Laboratory at Laramie, Wyoming, and that's where the selenium story started.

(laughter) **LATHROP:** Well, I'm not really sure about that. You want to know how selenium got started; is that it?

FISHER: Yes, tell us the selenium story.

LATHROP: All right. From my viewpoint, as far as nuclear medicine is concerned, it got started with Monte Blau . . . because he was looking for something that would localize in the pancreas, and the amino acids have a way of doing this, and he also wanted something radioactive. Sulfur does not have a radioactive isotope that was suitable, so he happened onto selenium-75; it worked reasonably well for those times.

HARPER: Well, it was as selenomethionine.

LATHROP: —yeah, as selenomethionine. He labeled the methionine with selenium in place of the sulfur.

HARPER: With the help of yeast.

LATHROP: Yes.

HARPER: It was a biological labeling.

LATHROP: Now, I guess this was about the time that the MIRD committee was working up to doing dose estimate reports, because, as you know, all the early publications were absorbed fractions of this, that, and the other thing that actually went into—

HARPER: Yeah. The selenium, of course, has a 120-day half-life. And in the study where you use selenium, you look at it 45 minutes after injection. So this is a little disproportionate.

LATHROP: We had access to the whole-body counter, so we decided that we would try to do a study. We did some animal studies, and we decided that we would try to do a study on Mr. Fields [a patient of Harper's] . . . we talked to him about what we were doing and the reason we were doing it [to understand its metabolism rate, retention, distribution, clearance, etc.].

HARPER: Well, he had the selenium scan. We administered 200 microcuries of selenomethionine

LATHROP: And it was just a matter of our making use of the selenium that he had; we didn't give it to him just for our purposes. As Paul said, it was for clinical use. But he came back. First it was day after day, I guess, and then it got to be intervals of weeks, and, finally, a month or so apart. And this went on for almost 3 years, and we were still able to get valid [radioactivity] counts. We had some problems when we started out with this research, because of the [low count rate] recovery of selenium that we were getting. We found that this was due to the placement of the detectors; that was useful, we then wanted to design a better-type instrument. Paul said something about the Poisonous Plant Laboratory. When I was living in Wyoming, I worked for the Poisonous Plant Laboratory. In the West, selenium was a big problem, because a herd of cattle would go through a pasture, and maybe half of them would die before they got to the other side of it because of the selenium in the soil that was concentrated in the plants that the animals ate. So I had that interest in selenium, too, which made it more interesting to me to do this study on a human. And that is the data, part of which made up the dose estimate report for selenomethionine.

FISHER: How is selenium evaluated in humans?

HARPER: Imaging.

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LATHROP: Well, no. I think he means if we did—were images made and looked at, or what kind of data of that sort?

HARPER: The only numerical data we got out of it was the whole-body count.

LATHROP: That's all we got out, but what about the people that were doing it clinically?

HARPER: Oh, they just looked at pictures.

FISHER: So the pictures weren't really used for—

HARPER: Quantitation.

FISHER: Quantitation and liver uptake.

HARPER: No.

FISHER: Fractional retention, retention half-times?

HARPER: No.

LATHROP: No, in those days, people were so happy to get an image; that was really all they cared about.

HARPER: Now, it's pretty close to the same today.

(laughter) **LATHROP:** Well, okay, yes, to some extent, because there are an awful lot of things that could be done with nuclear medicine besides making images, namely studying the biokinetics, pharmacodynamics, metabolism, etc., and natural physiological processes in the body. And they are not being done.

Thallium Research

FISHER: One of the interesting things that I came across was your use of thallium-199 as a heart-scanning agent.

HARPER: That's an interesting story.

FISHER: Now, you didn't have positron detectors at that time, did you?

HARPER: No. The "eye people" called me up one day and said, could I make them some radioactive potassium, because they had been reading. The ophthalmologists were interested in thallium localization, because thallium apparently localizes in pigmented tissues in the eye; it localizes differently in the eyes of white rabbits and black rabbits. They wanted to use radioactive potassium, because the potassium and thallium ions behave somewhat similarly, and they wanted to use potassium to trace thallium. We said, "My God, if you're going to trace thallium with potassium, you can certainly trace potassium with thallium." So we were off and running with thallium. We made some thallium on our little cyclotron by bombarding mercury. It was a horrible mix, and that's where the thallium-199 came in.

LATHROP: We couldn't make the thallium-201 in our cyclotron.

HARPER: We didn't have a big enough cyclotron. So we went ahead and tried it [thallium-199] on a couple of people. One of them was Mrs. Lathrop and one of them was a gentleman that had a melanoma. We said, "Aha, melanoma! This should tie in with the eye people, a pigmented lesion. It should pick up the thallium."

FISHER: Thallium has a half-life of 7 hours. That would seem to be quite suitable.

HARPER: Well, it was a mixture—I mean, if you bombard mercury, you can see what you could get. So we tried it and what did we get? A good picture of the heart. So that's what we presented to the Society for Nuclear Medicine, and that stimulated the people at Brookhaven to make thallium-201.

LATHROP: (to Harper) What we got [when you tried it on me,] was a great, big hot spot. You decided that my clothes were contaminated. . .Remember?

FISHER: What activity levels were used for these initial studies with thallium-199? For example, Katherine, you say you were a subject of one of these early experiments. How much activity would you permit going into your blood veins for this early study?

HARPER: A few millicuries.

LATHROP: Well, you know, it's not a matter, exactly, of how much activity. It also is what the quality of the activity is, average. . .But we had already—we must have done some animal experiments.

FISHER: It sounds like you were the subject of an experiment on several occasions.

LATHROP: Yes.

HARPER: We both were.

FISHER: Was this accepted practice, still, in that particular era?

HARPER: Still is.

FISHER: Still is?

HARPER: You don't give anything to a patient that you haven't tried on yourself, that sort of idea.

LATHROP: That's right. I would tell the people that I had asked to volunteer that I wouldn't ask them to do anything I wouldn't do to myself. And one day, one of the people I was working with said he really appreciated that. That was the reason that he decided that he would volunteer for the studies that we were doing.

Excerpted, with edits for sense and space considerations, from Department of Energy Office of Human Radiation Experiments interview with Katherine Lathrop and Paul V. Harper, 1996. Available at: www.eh.doe.gov/ohre/roadmap/histories/0472/0472toc.html.