NIDDK

Oral History Project

Interview with Dr. Herbert Tabor

Conducted on May 15, 2019 by Kenneth Durr

KD: This is an interview with Dr. Herbert Tabor, NIDDK. Today is May 15, 2019. I'm Kenneth Durr. Dr. Tabor thanks very much for taking some time to talk today.

HT: Thank you for asking me.

KD: I want to start with some background and go way back to when you got interested in science and how that happened.

HT: I was always, as far back as I know interested in science, but I wasn't sophisticated enough to know the difference medicine and science. I was interested basically in medicine, but in the research aspect of medicine because from our viewpoint now medicine was at a premature level at that time. And all the things we take for granted now, such as the treatment of infectious diseases, were in the future. I will always be interested in the interaction of science and medicine.

KD: In medical science?

HT: I didn't know the difference between medical science and science. We know now that the two are intertwined.

KD: Did you have the idea that you would go to medical school when you were in high school?

HT: Oh yes, definitely

KD: You started out at City College.

HT: That's right, yes. I started very early. I was, I think 14 and I didn't do any science there. I just took the regular curriculum and I was there for two years.

KD: Why did you leave?

HT: I had very good grades, and I knew I wanted to go to medical school. I discussed it with one of the Deans and he suggested that if I wanted to go to medical school I probably should go to a college outside of New York City because it was very hard for people in New York City to get into medical school because obviously the schools wanted a diverse population. So from there I went to Harvard for my second two years.

KD: Did you work with Dr. Baird Hastings?

HT: I started to do some rudimentary work when I was still in college. After I went to medical school I took the regular curriculum, and the first year had a very good biochemistry course given by Dr. Hastings. Then in my senior year at medical school I was in some sort of tutorial program and was able to take the last half year of my senior year and the next half year working with Dr. Hastings. In those days part of the class took a half year off before the internship , understandably a good idea since otherwise if a patient went to a hospital on July 1 he or she would be treated by brand new interns. Unfortunately, I think that's still a problem that on July 1st they're all fresh interns.

KD: So don't get sick on the 2nd of July.

HT: That's right. Going back to college, Harvard College had a tutorial system where you met once a week or once a month with a senior person usually on a one-on-one basis. My tutor was someone who had gotten his Ph.D. in science. At that point we discussed all kinds of classic science; so I continued keeping up with all of that when I got to medical school.

KD: Talk about the work you did with Dr. Hastings.

HT: It was somewhat esoteric. He was interested in the ions in the tissues, and he was particularly interested in magnesium, and I was working on it. And from there on, and this goes for a lot of work I did in future years, when I started a problem, I wanted to learn more about the subject without necessarily having any understanding of the basic chemistry. I was working on the ionization constant of magnesium phosphate, and that was the basis of my first paper in the JBC, that wasn't published until 1944.

And then when I got to New Haven, when I interned, I did a little work on the side and had another paper on measuring blood volume. That was not a major paper, otherwise when I interned there was no time for any more research.

KD: Did you do the regular clinical internship?

HT: Yes, internal medicine.

KD: At New Haven Hospital?

HT: Yes, that's part of Yale Medical School.

KD: Did you work with anybody, a mentor or anyone like that during your internship?

HT: No, but I interacted with a lot of the people and got to know them and discussed work with them, but there was no specific mentor. I was particularly friendly with Dr. John Peters. He and Van Slyke had just published a book on quantitative clinical chemistry.

KD: When you got your medical degree, did you go into the Commissioned Corps at that point?

HT: No, because I first interned.

KD: Right, after the internship.

HT: Yes. By the way, I might mention just for interest how I got into the Commissioned Corps. It was during the war and just at the beginning of the doctor draft. There were three uniformed services, Army, Navy, and Public Health Service. I was interested not only in research, but in public health. While I was interning, I heard they were giving exams for the Commissioned Corps in the Public Health Service in New York. Parenthetically, in those days being in the Public Health Service we were supposed to be willing or obligated to be assigned wherever you would be assigned, and not as in later years, know you could come into a place like NIH. So I went to New York and they had a board. I had to apply and I received a commission. To show how small the Public Health Service was, I was the 535th commissioned officer in the U.S. Public Health Service in the whole United States.

KD: This is during the war, so there must have been some assignments that didn't have to do with research.

HT: I didn't know that. I just had a commission in the Public Health Service. I would have had a year and a half internship, but the last day of my first year I received orders to go to Boston to sign in to the Public Health Service, and I was assigned to the Boston Marine Hospital. Three or four weeks after that I was assigned to a Coast Guard Cutter doing transatlantic convoy duty, because in those days unfortunately that was the most difficult period on the Atlantic. In the convoy was a ship torpedoed on my first trip.

Remember I had a medical internship, no surgery, and here I was the sole medical officer on this escort ship. One night, which was not unusual, one of the ships in the group of ships, there were usually 150, was torpedoed and went up in flames, and the sailors had to be rescued, and our ship rescued them. I remember the escort ship was very small, 327 feet. Fortunately, they were not seriously injured. But the escort ships, if they thought

they heard the sound of a submarine they depth charged it. I and a sister ship forced a German submarine to the surface and this was the first time during the war that had happened. The men on the German submarine had to escape into the water, and our ship and the sister ship picked them up, and brought them to my same sick bay, which was incredible. That was a very unique situation. They were on our ship until we landed in Scotland.

KD: How many missions did you go on?

HT: Three transatlantic. There were about 20 to 25 days each and the time in between was while they were getting together a new convoy. Because it was very important that this country was sending supplies to England and it was critical for the progress of the war. That was, I would say to put it mildly, very exciting, considering I didn't have anything other than a medical internship

Stepping back for just a moment, while I was interning, we received a small dose of penicillin sent from England that they wanted us to test experimentally because the British didn't have facilities to make the penicillin on a large scale. I and my fellow interns, two or three, administered the penicillin. This was the first case in this country of anybody being cured of illness by penicillin treatment. A woman had been sick, almost comatose, for months and suddenly—penicillin was miraculous. Then I collected the urine, because most of the penicillin is excreted in urine and it was sent down to Rahway, New Jersey for Merck to re-extract and then it was used for additional treatment.

Jumping way ahead, but quite an amusing story, is that maybe 30 or so years later when I was at NIH, one of the biochemical doctors was very friendly with me and we were discussing one thing or another. And it turns out that he, when he was working at Merck before he went to medical school re-extracted the urine that I had sent down.

KD: You found someone you had been working with and you didn't even know it at the time. Tell me a little bit about how you ended up here at NIH. Did the war end and then you were reassigned?

HT: No. Before I get to that I might mention something to show how strange it was being a doctor without a surgical background. On one of the trips, the convoy commodore—there was usually a retired admiral. This admiral had been commandant at Annapolis and he had acute appendicitis, so he was transferred to my ship by buoy until we got to Casablanca where they operated on him.

At the end of the third trip I got into port and I received orders to come to NIH, period.

KD: How did those orders come about?

HT: Here I'm extrapolating a bit, I think correctly. During the war there was a committee of medical research which was a subdivision of the OSRD, Office of Scientific Research and Development. There were a number of senior professors on it and also ex-officio, the heads of the uniformed services. The Director of NIH was taking the place of the Public Health Service director and he knew that Dr. Rosenthal was working on a war project involving electrolytes. I just assumed that somehow or another, that Dr. Dyer asked Dr. Hastings, who was on the committee, if he knew of anybody who had worked on electrolytes. That's a guess on my part. All I know is I received orders.

KD: So Dr. Rosenthal was here at the time?

HT: Yes, he was here for many years before that. He joined the Hygienic Laboratory when they were downtown at 25th and E. As you probably know, the NIH used to be called the Hygienic Laboratory, and they only came out to Bethesda in 1940. NIH was a small place then and it is amusing to recall the following as an indication of how small it was: so here I am, a young fellow just out of school, probably 22, and what do I do? I receive orders to report to the Commanding Officer. So I go up to Building 1, to show how different things

were then, and I go into the Director's office and say, "Here I am." Imagine trying to do that today. That was Dr. Dyer. He asked me where I was staying that night. There used to be a little cottage on the grounds and he gave me the keys to the cottage. I'm just guessing that's how I got here. All I know is I got orders.

KD: Were you assigned to work with Dr. Rosenthal right away?

HT: Yes, Dr. Dyer assigned me.

KD: What was his lab doing at that time?

HT: Dr. Rosenthal, who was an M.D., pharmacologist, because of the war was studying the treatment of burns and shock and was interested in finding out how you would treat a mass casualty because this was a real problem. Obviously if there's a mass casualty you couldn't have enough blood for intravenous and therapy, you couldn't have the personnel to give it. He was working with, I think mice and rats, and found that giving large amounts of saline could cure them, and that would be feasible. However, that was not an orthodox treatment at the time, and I assume that Dr. Dyer wanted to help Dr. Rosenthal and also to check on the findings.

KD: So he had already determined that saline could be useful for burns and shock.

HT: That's right.

KD: Were you replicating his experiments?

HT: And doing more. I was actually doing sodium and potassium analyses and explaining why saline worked. Parenthetically, it was rather interesting that this was rather unorthodox because most treatments accepted by the community required plasma and were based on experiments with one dog. Dr. Rosenthal, being a pharmacologist felt you had to have multiple animals to have a statistically significant result.

KD: What were the multiple animals?

HT: Oh, say 20 rats. Then we expanded the work to test traumatic shock and then developed a technique for bleeding rats, hemorrhagic shock. We could test and show that large amounts of saline would be a good therapy.

KD: Did that become the standard treatment?

HT: Little by little. At the end after the war, we also had another commissioned officer assigned to Dr. Rosenthal and he went to Lima, Peru to test this. The reason he went to Lima, Peru is they didn't have enough protein to administer, so he (Dr. Markley, who was working for Dr. Rosenthal) was able to test that large amounts of saline were important.

KD: Why was Peru the subject?

HT: Because it's a poor country and they didn't have the money to buy plasma or blood.

KD: They couldn't buy plasma.

HT: That's right. Finally the Public Health Service, one of their study sections, it took about ten years, recommended that this be the treatment for any mass casualty. Now it's well accepted that saline is important, although there is still disagreement about how much and when we should give it in general practice.

KD: You started working on histamine with Dr. Rosenthal as well.

HT: That's right.

KD: How did that come about?

HT: When the war started he had been working on, as a pharmacologist, histamine and picked it up again. Now an important digression here, which shows how small NIH was, I and Dr. Rosenthal were on the first floor in Building 4, which still looks the same, and on the third floor was the director of our division, equivalent, William Sebrell. Another commissioned officer had been assigned to him and Dr. Daft, who was working with nutritional supplements, vitamins particularly. Kornberg and I would work in the evening using the hemorrhage apparatus that Rosenthal had developed. This is of some relevance. I don't know if you're familiar with the name, Kornberg later got the Nobel Prize. We were very good friends because we worked together, and he had some other friends, and we started to have a seminar.

Then Kornberg asked to get additional training in biochemistry and was assigned to Severo Ochoa in New York where he learned a lot of biochemistry. When he came back he set up another seminar group that's classical to people in the biochemical area because it had some wonderful people who brought all kinds of new ideas including the idea that instead of working with whole animals you did enzymatic studies. By that time the policy at the Public Health Service had changed and we had a lot of good people coming as commissioned officers or foreigners. From there I developed and obtained an extensive knowledge of current biochemistry and we had seminar every day.

KD: This was lunchtime?

HT: Lunchtime yes. Even on some holidays. And using those techniques I applied it to histamine, to study the enzymes that metabolize histamines.

KD: So you learned these research techniques from your counterparts in the luncheon group.

HT: That's right.

KD: So the luncheon seminars were important for you to develop the mechanisms for doing your histamine research?

HT: No. The luncheon seminar was over in Building 2 and we covered all kinds of subjects. In fact, it's hard to believe now, but we covered usually everything in the biological part of Chem Abstracts. And ultimately with that knowledge I then applied it to what I was doing in Building 4.

KD: Tell me a little bit about, moving to the late '40s, where was your research going. You were working on histamine, you moved into histidine.

HT: This goes back to the seminar group too. One of the people in the seminar group had just come from Japan, Osamu Hayaishi, who was later quite famous in Japan. With him, I learned more techniques, and also learned that you can get more enzymes by using organisms like pseudomonas and growing them with the compound of interest as a sole source of nutrients. So we decided to test the metabolism of histidine. Hayaishi knew that there was a disagreement on what the first step was in the metabolism of histidine. One was breaking the ring and the other was deamination to give urocanic. And growing Pseudoonas with histidine as the sole nutrient technique and (doing some of it with Hayaishi) we found that going to urocanic was the first step in the metabolic pathway and that opened up a whole field of studying the metabolism of each of these compounds, in the further metabolism of histidine.

KD: No one had worked out those out?

HT: Not yet.

KD: Folic acid is involved here, somewhere too.

HT: That's right, one of the steps in going from one of the intermediates, formiminoglutamic, to formic, ammonia, and glutamic. And we did that with Jesse Rabinowitz and with another person in the Building 3 lab that at that time was headed by Bernie Horecker because Kornberg had left to become the head of a department at Washington U.

Jumping ahead, we were also good friends with Howie Hiatt who was also in that group. He had just left to become a professor of medicine at the Beth Israel Hospital in Boston. We got the idea that if folic acid is required for that step you could use that to measure whether therapy in humans—whether the therapy worked with the people who were taking it, and sure enough that was the case. Especially if you gave histidine normally you wouldn't get any formiminoglutamic. If they weren't taking the medication, then you got formiminoglutamic.

KD: So you could test the efficacy of folic acid? Was that what you were able to do?

HT No, we were just testing whether they were excreting formiminoglutamate or not with an indication whether the patient was taking the folic acid therapy.

Also, I should emphasize that each of the items that we've talked about would take a year or two. You had to develop methods and you didn't have the techniques that we have now, of all kinds, which is certainly another very relevant story.

KD: I read somewhere that you had to make your own glassware at some point.

HT: That's right, just blow your own.

KD: Dr. Rosenthal is spearheading all this. This is still his lab.

HT: Yes. But his approach, which I think is very important, was to allow people to both work on things he's interested in, but also if they have their own ideas he lets them do it himself. And that's a rather important point to make in the history of NIH, because NIH was very good in allowing that, especially when everything was small. Dr. Rosenthal, for example, had at that time a young postdoc, Jack Strominger, who later became a top professor at Harvard, to work on his own project.

KD: Yes, so we were working through the histidine metabolism research.

HT: Yes.

KD: The next step seems to be heading into the amine investigations, looking at amines. Did one lead naturally to another?

HT: No. The important thing is most of our work in recent years, recent meaning 30 years or more, was on spermidine and related polyamines. And how we got into that, and this again shows the beauty of not only Dr. Rosenthal, but of NIH at that time. Dr. Rosenthal was just reading in the library. He was reading a German book, *The Biogene Amine*, I think by Guggenheim, and it described spermine. Spermine parenthetically goes back 1670-something with Leeuwenhoek discovering it. One of the first objects he saw, he saw crystals in his new microscope. There were scattered papers since that time and Dr. Rosenthal decided there was enough to tell him that it was a widespread compound.

So he reached a conclusion, especially since he was interested in amines, that any compound that was that widely distributed must be significant. As a pharmacologist, he injected it into mice. But instead of just watching the mice for one day he watched them for a week, and they all died. In other words, spermine was toxic. So we started working on it to try to figure out why it was toxic, and that's the beginning. We then decided, especially with the background of that seminar group, to do everything we could to learn how it was made and how it was metabolized.

KD: Your wife was working with Dr. Rosenthal on this subject as well, is that right?

HT: Yes, but not until 1953 because with her background she was able to help him.

KD: Take me through some of the steps and high points of the research.

HT: That's a difficult question and almost contrary to what I've been saying. Most of the time we were not interested in the high points, we were just interested in how things worked. In this case, we first showed that putrescine, which is a four-carbon diamine, could be converted to spermidine with methionine. Then the next step was to show what's the intermediate, and we showed adenosylmethionine, which was a compound that Guilio Cantoni had worked on for methylation, could be the source of the three-carbon amino propylamine part, but before you could use it, it had to be decarboxylated.

By the way I might mention as a general summary, there were only a few papers in the Index Medicus when we started on spermidine and now there are 16,000 papers in putrescine and spermidine. And to put it mildly, I haven't read most of them.

KD: It looked as if the research project was stepped up. Did you get more funding or you were bringing more people in during the late '50s?

HT: No.

KD: How many folks were working on the spermidine?

HT: Usually one or two. But then we also had other people in the lab. Most of the time when we saw they were capable, I followed Dr. Rosenthal's footsteps and let them work on whatever they wanted to, and some of them really did some outstanding work, like Bob Schimke and several others.

KD: What did Schimke do?

HT: He studied protein turnover in liver and hormonal control. And there were any number of other people such as Loretta Leive, Chet Berlin, Chris Raetz and so forth. They don’t show up in my bibliography because they published on their own.

But in general, we had random studies in-between. If we had some idea we would want to follow it up sometimes it would lead somewhere and sometimes it wouldn't. Or sometimes it would lead in ways that were unpredictable. While looking up my reprints in preparation for our talk, I was reminded of some work we did with Dr. Demetrios, who came to work with me and later went to Western Reserve.

Normally when you're testing two proteins or two things for antigenicity, I'm talking about several years ago, I don't know what they do now, you would give them a dose of radioactive material and wait probably several weeks to see what happens. We got the idea of measuring ornithine decarboxylase and we found that if two proteins are incompatible they immediately had a high CO_2. Even though this method never was used, the idea was good. Another example of random studies is, and this is one of the things Celia my wife did, we developed methods, and that took quite a lot of time, for determining amines chromatographically, together with some coworkers. Celia then showed that if you let the cells grow old the putrescine is converted to glutathionylspermidine. We didn't do any more with it. But another group independently had found that you had to have glutathionylspermidine spermidine for glutathione to work in trypanosomes. So for a while this was the basis of some therapy for trypanoomiasis.

KD: One of the things you talked about was the fact that people in the lab could study whatever they were interested in, which raises the question, when you joined the laboratory of experimental biology, at some point it turns into NIAMD. Was there any organizing leadership that was driving the research at any point in your career?

HT: No. Our institute has always been very good in giving my lab or the successive labs freedom to do what they want. And this is true now, too.

There is one thing I wanted to be sure to mention as an indication of how good our institute has been and how it has led to good results, and that is my successor as head of the laboratory is Reed Wickner, who had come here as a postdoc right out of medical

school and who parenthetically also went for a year of training elsewhere. He got the idea that he should work on yeast and has developed beautiful work in yeast. I wanted to be sure to emphasize how important Reed's work has been. He was able to do this because he was able and was smart enough to take advantage of it. He discovered something really unique and that is yeast contained something called prions. Prions are a way that proteins can carry out information without the involvement of a nucleic acid, and that's a fantastic finding and leading to all kinds of work. I think it's very important in indicating how good our institute has always been.

KD: Let's change up a bit and talk about NIH on a broader scale. Tell me about working with your wife. It seems unusual to work together as scientists.

HT: I could say it was unusual, but it worked very well. We had a lot of good papers and parenthetically four children. It's beautiful. By living this close I can come over before breakfast to put some cultures on and so forth. And we could discuss the work. I'll give her credit for things working.

KD: Speaking of culture, you talked about the luncheon seminars, but what was it like living and working at NIH in the '50s?

HT: It's changed a lot. The reason they have these houses is that when they built NIH they copied the setup from one of the Marine hospitals, which was a Public Health Service hospital. When we moved here the Clinical Center was not even started, so there were just a few buildings and the director lived on the station, and all the other people at that time were commissioned officers in the Public Health Services.

KD: Did you move here in the '40s?

HT: Yes, late '40s, or very early '50s. Then gradually things changed. But it was very nice then because I got to know and discuss things with people in different fields. Later, it

gradually opened up to anybody who applied. There were so few houses. Now all are being converted into offices.

KD: How many people lived here on campus back at that time?

HT: I think a dozen. A dozen houses, something like that, two big ones and a number of smaller ones. The director lived here and that was good from his point of view, too.

KD: The director lived here? So he could keep tabs on people.

HT: He didn't have to.

KD: Did you succeed Dr. Rosenthal as director of the lab?

HT: Yes.

KD: How did you run things and mentor people?

HT: The answer to that is I didn't. We tried to get the best people we could to work in the lab and some of them worked on my project, but usually I encouraged them to work on their own project, and that's about it.

KD: Did you spend most of your time working at the bench?

HT: Yes, all the time.

KD: I think we've hit the point where we can talk about the journal.

HT: Before we get to the journal, there's more general stuff to talk about and that is the equipment. The need for expensive equipment and the need for supporting personnel has changed over the years enormously. What I've been talking about is, in a sense, the old-

fashioned approach. Nowadays, you have to have expensive equipment, such as fancy mass spectrometry or crystallography. In addition, there have been other changes, many of which are expensive. For example, you mentioned what my wife was doing, for example. She did a lot of DNA sequencing that was very time-consuming. Now you want a sequence? You put it in the mail, and the next morning you get a sequence. It's enormously different and this makes a real difference to the people who are running things that they have a bigger operation to work on. I think that's an important difference.

The same thing is true with medicine. Now you can study a lot of medical problems in cell culture, which means you can know much more about what to do.

KD: When did you first become editorially involved with the journal?

HT: I can't tell you exactly when because at one point I was just one of the editors. Then about 50 years ago I became editor.

KD: 1969.

HT: Something like that. Interestingly, all my work I did with the journal was in the evenings. Because of government rules. That was an outside activity, so I did everything after I got home. And that was exciting because I got familiar with a lot of publications and a lot of work.

Today is an interesting day. I told you my first paper in JBC was in 1943. I just got a paper accepted by *FEBS Letters*, a different journal, so I'm still publishing.

KD: Congratulations.

HT: One thing I always mention, it's been very exciting to be in science and medicine at this time. It goes way beyond anything we could have dreamed on when I was at school, and what more can I say.

Even though I did the journal in the evening, the journal has expanded enormously and the number of papers and editors has expanded. But the most important thing and one that I am, with two people from the staff responsible for, is the electronic distribution of information. Because when I first started with the journal, in the evening or late afternoon, all the reviews were on paper. Actually, a bag was brought over to me every night to work on. It took months for information to reach foreign countries and vice versa. Now with the help of the journal staff and editors, we have gotten to the point that we now have all the publications distributed online, this was the first biological journal that did that. In fact, we don't even print the journal on paper anymore.

KD: You started by putting it on CD-ROM.

HT: We started with CD-ROM, but then with the help of the chief librarian at Stanford, he was imaginative, and we were very enthusiastic to say that CD-ROMs were not the answer. It was inconceivable before, but now all over the world they can read what somebody here is working on, and vice versa.

KD: Are you still associated with the journal?

HT: Yes, two nights a week I assign papers, but pretty distantly. That was a big thing even though it was an extra-curricular thing, I think it was important.

KD: Besides the electronic transmission, how else has the journal changed?

HT: We tried not to basically change. But I think now, in general, the articles are longer and looking for mechanisms. But I feel, and I think the journal feels, that we don't want to lose sight of the fact that we want to publish good scientific work, whether it adds up at this time to a mechanism or not, but with the concept that if it's good scientific work, that will be important.

KD: Is there anything else you think we should talk about?

HT: Oh, hundreds of things.

KD: Looking back at your career, you talked about your education, the people, and the circumstances that led you down certain paths. How much of your research path through your time at NIH has been self-directed and how much of it has been due to chance—circumstances?

HT: We never know that. One thing leads to another. If you're working on a problem where you're intimately involved, then you do the next thing that seems to be best. If you get the idea from something you do that you follow up in a certain way, you might say it's due to chance, but it's not really chance, because you wouldn't have made that conclusion without a lot of work ahead of time. Here again, coming back to the work that Reed Wickner is doing, he reached this conclusion based on a lot of work that he had done with yeast. If you came in from the outside you'd say it was just chance, but you had to have a fertile background to take advantage of it.

KD: Well, Dr. Tabor it’s been a delight talking to you. Thank you very much for your time.

HT: Thank you.