

David Rall, M.D., Ph.D.
Retirement Interview
No Date

Interviewer: In 1970, you were a 43-year-old cancer researcher at the National Cancer Institute, well-launched in your career and at a world center of medical research in Bethesda. Was there a particular moment or sequence of moments that turned you toward an interest in environmental health, even before you were approached about the position in North Carolina?

David Rall: Two different things happened in the year or so before that. I had gotten very interested in how you predict toxicity for individual patients. At the cancer institute, I was involved in developing anti-cancer drugs, which are very toxic and must be used at very close to a dose which gives serious toxicity. The whole idea of how well laboratory animals predict for human effects was high on my agenda even then. About that same time, the FDA had come under attack and then-Secretary Matthews set up a committee to review the FDA. Nope, it was an earlier committee than that. Secretary Finch had asked for a review of prescription drugs, which was done in '68 and '69, and that brought up some issues of how the FDA functioned and whether there was enough science in the FDA.

I was asked to set up a committee within the Public Health Service to review the functioning of the Food and Drug Administration. This I did. It was about a six-month job and I was detailed downtown. This gave me the first sense of what one could accomplish in the scientific political arena. I put forth what I thought was a very good report. At the same time, Charlie Edwards was appointed as commissioner of FDA and obviously Charlie's appointment had considerably more impact than my report, but the main thing is the FDA reviewing officers need time to pursue some avenues of research and scholarly endeavors, and unless they have that, FDA will forever have problems reviewing and approving drugs.

Also, I would like to have seen drugs rereviewed at certain intervals, and I suggested that could be done by outside consultants, and I have just heard in the last week or two that the new FDA committee is recommending outside consultants for that.

Interviewer: It's taken that long to come around?

David Rall: It just keeps coming around. The more I thought about it, it became apparent that although one could probably predict for individual patients under careful medical care of the toxicity of certain drugs or therapeutic agents, the question of population toxicity was unresolved. That is, if the whole population is exposed to a toxic chemical, even at a low dose, what will the response be? Will a low

percentage, still perhaps a very large number of people, be adversely affected? It was my taste of the power in HEW North, the presence of an extremely able assistant secretary, Roger Egeberg, and my concern about the population toxicity of environmental agents that made me really very interested in the job that Dr. Marston [NIH Director] offered.

Interviewer: When you joined the institute, it was quite small and located in what must have seemed like remote North Carolina. Clearly, you saw the opportunity. Did your colleagues, mentors, and family unanimously share your enthusiasm?

David Rall: No, I think everybody was surprised when I said I wanted to go. Carl Baker said, "I never thought you'd do it. I bet everybody you wouldn't go." It just seemed to me that here was an opportunity to build an institute that is really very rare indeed. I must say, I'm glad I made that decision.

Interviewer: What was the most difficult thing for you about leaving NIH in Bethesda, the campus there?

David Rall: The fact that you miss the easy frequent association with a large selection of the best biomedical scientists in the world. Living and working on the NIH campus you can see somebody who is expert in almost anything in biomedical research. Many of our most productive research ideas came from informal seminars that we were able to set up, crossing all institute lines. This was a severe loss and it's taken really almost 20 years to rebuild here at NIEHS enough of a critical mass of scientists so that we approach that down here. We certainly don't have it because we only have a few hundred scientists instead of a few thousand, but we're in good shape.

Interviewer: Just a follow up question on that. Does the university and Research Triangle Park community here in some way compensate for that?

David Rall: Absolutely, absolutely, but it's not the same. You do have to drive 10 miles or more, and that's a threshold of effort that is not the same as "Let's meet for lunch in the cafeteria in Building 1 or Building 31." That's almost effortless.

Interviewer: What was the greatest short term challenge you encountered on arriving in Research Triangle Park?

David Rall: One that should be familiar to everybody, and that's personnel slots. In those days, we had freezes and we had cutbacks and everything. The problems were exactly the same. I think none of us realized how inadequate the facilities were. Actually, the north campus is very pretty and very charming, but the large number of small buildings tend to promote an insular behavior and prevent the easy flow of ideas

from group to group. The same problems we have today, personnel slots, travel money, and big equipment money.

Interviewer: The late Dr. Norton Nelson of New York University was another longstanding friend of the institute. Did he offer suggestions early in your years as director that were especially memorable?

David Rall: We all worked with Norton as if he was a member of the family. Norton's overriding suggestion was hire the very best scientists you can get. He was a great help to me, particularly early, because I really knew very little about air pollution and some of the other classic environmental health issues. He made it easy for me to learn and get into the mainstream of the typical environmental issue. The institute lost, I think, its best outside friend when Norton died last February.

Interviewer: What were your own priorities in assuming the directorship, to the degree that you can say? What priorities have changed and what have remained?

David Rall: The biggest priority has to be having a very solid scientific base, hiring and retaining the best scientists we can get. I think NIEHS, as some of the categorical institutes, has an additional function other than pure basic research, and that's the applied research that makes it categorical, that gives it a function over and above general biomedical research. We need to do research that not only is at the cutting edge, but we need to do research that provides practical answers to important problems. The second most difficult job, after you've gotten good scientists, is to keep the balance of applied research and basic research. The groups tend to be a little wary of each other, and you've got to convince them that they can work together, and when they do, the results can be spectacular. Our ability now to use protooncogenes, oncogenes and so forth, suppressor genes coupled to our animal toxicity testing effort is truly a spectacular thing.

Interviewer: The development of South Campus could take up an entire interview all by itself. Perhaps you could offer just a synopsis of how the idea for the new buildings became a reality.

David Rall: It started in a place nobody would ever guess — in a bar in Greenwich Village with country music playing as the featured attraction. I was there with a number of other people: Dave Ogee and Scott Philip. I asked Dave and Scott, "Tell me, how can I get the money to build a permanent facility for NIEHS?" They outlined the two, three things that you need. You needed support from the appropriations subcommittee, you needed local support, and you needed support from the state delegation. If you could get all those three, they thought that it would be possible. I then was able to talk to Wattsville Sr., who was marvelously supportive of this idea. He and L.H. Fountain, who was then the Congressman, really made it possible that we could get the funds for the building in which we're sitting today.

If you want to look back, you have to realize that first, the appropriation was split, so they only funded about half the building the first year and the other half the next year. The other complicating factor is that both appropriation bills were vetoed, and so the veto had to be overridden, and it was in both instances by both houses, and so the building we're in today really had a very difficult birth. I think it was worth it. Now we're well on our way to getting additions to this building, which will let us move out of North Campus and give it back to the Research Triangle Foundation. I should add that the Research Triangle Foundation really was a marvelous help in all of these difficult negotiations.

Interviewer: I wasn't aware of the vetoes involved. That must have been suspenseful. You have had to become something of a self-taught scholar of the Congress on top of being a scientist. Was this an innate interest for you or something that happened in the line of duty?

David Rall: I was always interested, but I became much more interested as I took over this job. It's simply important that you understand how Congress works and understand how congressmen and senators work. It's an institution that is often criticized, and it should often be criticized, but when you try to think of a better system, there simply isn't any. It is, in fact, responsive to the people. People have to learn how they can exert their influence, because every other lobby learns how to do it. I think it isn't a bad system. It's great fun to watch and it's really a very exciting game to play.

Interviewer: We've heard a lot in recent years about the politicization of appointments in federal research agencies. Do you see this as a trend, and if you do, does it concern you?

David Rall: I've always thought that there needed to be a little more care in organizing federal agencies which have a large research component. Obviously, the policymaking people in those agencies have to be political. They have to respond to the current administration. But, I had hoped there could be at the next level a senior permanent scientist who was apolitical able to work with either party. There has been some politicization of NIH. I don't think it's all that much. I think the problem with NIH is that we've simply been over-layered. Twenty years ago, 10 years ago, the NIH director and most of the institute directors had easy access to the Secretary and there were dialogues all the time and constant access to the Secretary's chief advisor. This slowly disappeared, and now NIH is really buried at the bottom of a very large bureaucracy. None of the bureaucracy, it seems to me, really wants to give up any of its power.

This means that NIH is going to be in for a very difficult time, unless one of two things can happen. It can be moved out of the Department of Health and Human Services, or else the Department of Health and Human Services becomes the

Department of Health, and NIH would therefore be one of the three major components of such a department. Or, the intervening bureaucratic layers magically and unexpectedly were able to be melded so that the NIH director could have a much closer access to the Secretary, and much more of their own decision-making power. It is perfectly preposterous for the Secretary to have to approve or disapprove of the appointment of a world class scientist as a member of SES. Not a policymaking position, but simply running a laboratory or running a section. For this to have to go beyond the director of NIH is a monumental waste of time.

Interviewer: There's a lot of follow up questions I could ask on that, but I guess I'd better stick to the script for the sake of the length, but that's fascinating. In 1978, you became the founding director of the National Toxicology Program. How did the NTP come about?

David Rall: On a cold and snowy morning in February, I got a phone call from Rick Cotton, who at that time was one of Califano's executive secretary assistants. And, Rick said, "You know, Dave, we just had a meeting with Joe and it's a shame you weren't here. Art Upton, Don Fredrickson, and I, and we all decided that NCI shouldn't be in the business of doing all the animal cancer testing and there should be a much broader toxicology program within the department." That then started a great flurry of proposals, of counter-proposals, of memos back and forth. Somebody in the circle of this exchange of memos seemed to slip them to the blue sheet, so if you look at the blue sheet from February '78 on through November '78, you can probably follow the development of the NTP with great precision. It was then just a matter of negotiations, primarily between us and FDA and NCI. I think it got set up in a reasonable way and has worked very well.

Interviewer: Its establishment happened very quickly, it seems to me.

David Rall: The first idea was February and it was established in November. It was established both by a permissive act of Congress, it didn't say "Thou shall ..." It did say, "The Secretary shall." At about the same time, the Secretary did. So, we kept the appropriation and authorizing committees completely informed, and they were entirely in favor of the whole idea.

Interviewer: What do you see in the future for NTP? Changes, expansion, new directions?

David Rall: No, I think it's going to go pretty much the way it is. We do have collaboration with the other parts of NTP. Mostly it is the NIEHS budget and I don't think that's surprising. I think it's probably appropriate. The changes will be scientific. As we learn more about those steps in the mechanism of carcinogenesis, we'll probably be able to develop much better, quicker, and hopefully less expensive ways of assessing the potential carcinogenicity of chemicals. I think we need some more money to test a few more compounds a year than we're doing now, but I don't

think this is major. The changes will be scientific, and I think they will be very important over the next three or four years.

Interviewer: Just check this. I don't want to break in the middle of a question if I possibly can help it. We're about halfway through the first side. That detail I did with NTP is fascinating in terms of the philosophical discussions going on. You've decided your time between the RTP and the Washington, D.C., area. Have you ever computed your air miles and how has this worked out for you? Most people might not like it.

David Rall: It's very interesting. Having lived in Washington for, I guess, 17 or 18 years before I came down here, I didn't really understand or know Washington until I became a visitor. When one has a family and lives out in the suburbs, one tends to stay out in the suburbs and not enjoy as much of downtown Washington as you could. In all honesty, I got very tired of the routine of parking, getting on the plane, getting off the plane, trying to rent a car, and so forth and so on. Life for the commuter really deteriorated after I came down here. You may not remember, but in 1971 you really didn't have to go through the terminal to get on the plane or get off it. There was no problem parking in the main parking lot. That was very nice. The Eastern blue room was very convenient. Eastern was a very good airline, and in the early days, commuting was really more hassle-free than it was lately.

Interviewer: This is the international question that goes on and on, but you've recently visited Japan to help commemorate the U.S.-Japan Cooperative Agreement on Health and the Environment. You've received medals from the Finnish government, from the Ramazzini Society based in Italy. Other NIEHS international agreements are with Egypt, Germany, the USSR, China, Taiwan, some others, as well as the World Health Organization. You've just been appointed to the WHO Commission on Environment and Health. The globalization of the environmental health effort — could you say something about the challenge for the future? Seems as if we're at the beginning of a very long road.

David Rall: We have come a long way, too. There are environmental health problems of the developing countries — of course they are very different from ours. I've been very concerned about that. They don't need trained research scientists. They don't need to do much research. What they lack are the mid-level scientists who can understand and interpret scientific data, toxicology data, and apply it to their own situation. The International Program on Chemical Safety was set up in part to do this, and I think it's not done a very good job in training that sort of third-world scientist. I hope I can push harder on that in the future. It is important to understand that the regulations that we have in our developed society may not at all be appropriate for a developing society. They really have to set their own

regulations, but they must have the best possible information, and they must have people who can interpret it in the light of their own needs.

The other thing that has made it really a more globalization is the fact that we're seeing in a way that we only dimly saw before that environmental health is an international problem. I remember very clearly the scientists from Great Britain coming over and assuring us that tall stacks were very effective, that they had very little SO₂ problem, and that we smiled and agreed, mostly by not saying anything. And, the people from Scandinavia came over and told us about how all the SOX came from Great Britain and Germany and was deposited on Scandinavia. The fact that there were these global aspects did not really seem to impress anybody until two things happened: the ozone layer problem and the CO₂ buildup. Both of those were discussed here at a Fogarty meeting shared by Margaret Mead in 1975, and I'll get you the date on that.

They laid out, amongst other things, these two potentially serious problems. People, who talk about the surprise or the shock of global warming, or the ozone UV problem, simply were unaware of the literature. It was quite clear these were potential problems about 15 years ago. We didn't know how bad they'd be, but clearly a lot of people started tracking that far back. I think those two truly global problems have focused the whole world on environmental issues. I look forward to the WHO Commission. I think it will be very important, at least, to prepare its report in time for the Environment Conference in Brazil in '92. You remember the first UN Environment Conference in Stockholm had almost no input on environmental health. It was all about the environment, and this will have, I hope, a major input from this WHO Commission on Environmental Health. It's going to be interesting to see how it all comes out.

Interviewer: You said that one of NIEHS's principal missions is the training of professionals in environmental health science. This is not an easy time for young scientists. What are the challenges for the future in the area of training new professionals?

David Rall: The worst thing that's happening now is the federal budget, the talk of ramrodding and the talk of a 30% cut and so forth. The 30% cut isn't going to happen. It simply won't. This is sending the wrong message to young scientists, that don't get into biomedical research because it's an unstable field. This is potentially a disaster. If we don't get a selection of the brightest young kids as they come out of high school and college to go into biology and biological chemistry, and get into graduate school or medical school, we're going to be in deep trouble in 15 to 20 years.

There are two aspects to this. One is simply the understanding and eventual prevention and amelioration of disease, which is the function of NIH. The other aspect is very important in terms of the economic success of the United States.

We no longer can produce automobiles at a competitive cost. Maybe automobiles, but certainly not big steel, and some of the other simple basic manufacturing infrastructure activities. What we have now is the best group of biotechnology companies and scientists in the world. We can make the enzymes that are in our bodies, and the plants and animals, do almost anything we want, and this is going to be more and more important as time goes on. The ability to create enzymes, and to find an enzyme that does something useful in some strange form of life, and to be able to make that enzyme that you may first find in a snail work on a commercial large scale production line, is the future of biotechnology, and it's going to be very important to the United States. We need the bright young kids to do that.

Interviewer: Is there any one trait you look for in young scientists that indicates to you that they have what it takes to do excellent science?

David Rall: I think it probably takes more than one trait, but you've got to be extremely curious. You've got to be asking questions, not always the right one, but ask questions, and you've got to be willing to work to get the answers.

Interviewer: We hear a lot today about big science — large organizational efforts involving large budgets and thousands of staff members. How does this kind of science relate to the cultivation of individual talent and creativity in research?

David Rall: I don't know that it has anything to do with that. I think big science is necessary now. I certainly think we have to be very cautious about launching very large programs. They develop a life of their own. They can take up inordinate amounts of dollars, and they're very susceptible to problems. As we've seen, I think, from NASA's problems in the last five years that the management of a large scientific program, like the Hubble telescope or the space shuttle, requires an almost unbelievable amount of managing ability and it's very hard to do those successfully. There is a place for big science, but I don't think it should overshadow the more traditional science. I think it's clear, however, that it's increasingly difficult for an individual scientist on his own to be quite as effective as he was 20 years ago. This means teams of two or three or four, but not two or three or four thousand.

Interviewer: How would you compare starting out today as a postdoc with being a postdoc in the mid-'50s?

David Rall: I don't know. I suspect it's not all that different. There are a lot of advantages. If any of you want to remember back and trying to get 10 clean carbons from a manuscript to go to some of the major journals that was a major technological hurdle. I think the scientist still operates the same way. You need to know the literature. You need to find good questions. You need to identify questions that

are answerable. You need to keep your eyes and ears open for new information, which will let you develop a hypothesis or do an experiment. You need to be aware of what's going on in not only your own field but ancillary fields. Now you need to know a lot more about a lot of things. The database increases constantly. But, we were saying that 25 years ago, so I really don't think things have changed very much.

Interviewer: In terms of personal satisfaction, what are the three or four accomplishments you think of first when you look back over your years at NIEHS and why are those particular ones?

David Rall: In no particular order, I think the final understanding that lead is very much more toxic than we thought it was for a while. This could have simply an enormous effect. I am constantly worried that in the inner city, in older housing, we're condemning a great number of children to a life with less intelligence than they were born with. This may, in fact, be one of the causes of some of the inner city problems, and I simply think that we must pay great attention to lead in the inner city and, of course, wherever it's found. I am concerned about old farmhouses. I think many of these probably have enormous amounts of lead paint, and individual families that have serious problems. I think we've provided, now, information on how toxic lead really is. In following up on this, there's basically not much NIH can do. It's really up to the other agencies and the Department of Housing and Urban Development. On the other hand, I think our role will be to keep pushing for more attention to the lead problem.

If you look at the animal toxicity testing, we have developed, really, a very solid mechanism for doing that, the various quality control measures, the pathology review groups really now are state of the art. Animal testing, although it's often criticized, is still absolutely invaluable. The grant-supported work on understanding air pollution is also a monumental report. Soot and SOX have been used as the index for air pollution for a long, long time, and they've done a pretty good job. But, many of our grantees have now shown that there probably is the hydrogen ion, the acidity, and it's that and independently ozone, and the two of these may really be the culprits in the typical air pollution that we have. Once we clearly identify these, it may offer easier ways of controlling some of the air pollution problem.

The whole series of efforts on dioxin and TCDD and PCBs, this institute has been a leader in this. I think we've laid out the potential toxicity of these compounds. We have not gone on the extreme of saying they're just terrible and so forth. Some of the epidemiological studies that we've done have shown that PCBs can have a deleterious effect, and we have some pretty good idea of what levels have caused those effects. I'm impressed that the recent work on end stage renal disease, and identifying specific chemicals or lifestyles which lead to increased renal disease,

can have an enormous important effect on human health. The work on the diethylstilbestrol and its role in male sterility, and the problem of estrogen in the environment are very serious.

As I said earlier, the coupling of the molecular biology of oncogenes with the practical technology of chemical testing, I think, will yield many, many benefits and one could go on and on and on. I think NIH has accomplished a great deal.