

Dr. Henry Metzger
July 30, 2001

This is an interview with Dr. Henry Metzger, July 30, 2001 at the NIH campus in Bethesda, Maryland. The interviewer is Sandeep Khot. The interview is in regards to Dr. Metzger's reflection of the Research Associate Training Program at the NIH when he was here in 1959.

Khot: When was the first time you heard about the Associate Training Program at the NIH?

Metzger: It was either my senior year or my internship, probably my internship.

Khot: And from whom did you hear about it?

Metzger: I couldn't tell you.

Khot: What was the perception of other medical school professors or classmates or interns, I guess, toward the program?

Metzger: It was very positive.

Khot: Very positive?

Metzger: Yes.

Khot: How important was the doctor draft in your decision to come to the program in 1959?

Metzger: Well, it certainly was an important consideration. In my own case, I'd pretty well decided that I was headed for academic medicine, so that decision wasn't influenced by the doctor draft, certainly. Whether I would have tried to come to the NIH had there been no doctor draft, hard to know.

Khot: Would you have stayed in academia instead of coming to the NIH if there were not a draft?

Metzger: Potentially. Well, I mean, in the sense that I knew that professionally, that's where I wanted to end up, doing teaching and research. I knew that. But I haven't really given any thought to exactly where.

Khot: Okay. Can you comment on whether the fact that the NIH was somewhat of a bureaucratic federal institution detracted from its appeal when you applied in the late '50s?

Metzger: No, it had no influence.

Khot: No influence. So it was still an attractive place. Although it was a governmental place, it was still pretty attractive in terms of continuing your career.

Metzger: Yes.

Khot: Considering the high level of competition, how important was it to have some sort of connection among like your professors or attendings? Did you have any connections with anyone you were doing research with who knew someone at the NIH and was able to refer you?

Metzger: Not that I know of. I think certainly the professor of medicine had connections, quite close ones, with some of the people at the NIH, but I don't know... I think this affected their opinion of the NIH, but I don't think that they intervened in any way.

Khot: Okay. How common was it at the time for physicians to forgo a clinical practice for the opportunity to solely conduct biomedical research?

Metzger: Well, first of all, the fact that I chose to forgo clinical work for research, I think even among my peers, that was a little bit unusual. I don't know, in

fact, that anyone else in my class gave up clinical work altogether. Most of them continued to do some clinical work. At Columbia, where I went, that was the idea of doing research and going into academic medicine was certainly more common than at many other institutions, although it was still a small percentage of the class. I think in my class, at most about 10 percent went into any kind of academic medicine.

Khot: Were those, in general, the higher AOA or was it all...

Metzger: I can't tell you that.

Khot: Okay.

Metzger: I have no idea.

Khot: Okay. Can you describe the research training environment at the NIH when you arrived as a research associate in 1959?

Metzger: Well, I think one major difference between that time and now is that the research groups were a lot smaller, so that one tended to have a more intimate relationship with one's supervisor than one tends to have now. In my own case, I was the only postdoctoral fellow. There was a technician, what one would now call a staff scientist, the principal investigator, and me. It was a three-person laboratory, and that would be a little bit unusual nowadays. The principal investigator under whom I worked had no office. His desk was in the laboratory, and my desk was right next to his desk. So I literally saw him all day and every day.

Khot: That's much less so now?

Metzger: Yes.

Khot: Do you think that open-door policy for just kind of the... I know others have commented on just the informality of being able to work at the NIH in the '60s, there was somewhat of an open-door policy, or you called your principal investigator by their first name and that kind of congeniality. Do you think that was more so then than it is now?

Metzger: Only in the sense that there tended, I think, to be smaller groups, although I should say this, that I was in an institute that almost prided itself on having small groups. In other words, it certainly considered itself probably the most academic-like institute. That was the original Arthritis Institute. And probably that and the Heart, Lung – at that time it was just the Heart Institute – sort of were a little bit more, had a little bit more of an academic atmosphere than others. But in terms of calling your supervisor by first name, that's still the case here. So it still is not a terribly hierarchical organization, although that varies from institute to institute a little bit, but it varies more in terms of the style of particular individuals, I think, more so than something that's from the top down.

Khot: Other associates have commented on how the associates “taught each other” their respective fields. Can you describe any special collaboration in which you participated as a research associate and which you learned your field from other associates?

Metzger: A little bit, yeah. There were a couple of associates. I was in a laboratory that was a protein physical chemistry-oriented laboratory, where the principal investigator had no particular interest in or, certainly, experience

in immunology, immunochemistry, and yet that was clearly the direction I was moving in, so certainly in, particularly, my second year, I interacted with other postdoctoral fellows or research associates interested in immunology to a considerable extent.

Khot: Okay. Was this flexibility something that you felt was pervasive throughout the program?

Metzger: I think so.

Khot: Is this approach still present today where I know there are no longer any research associates, but still that sense of flexibility in principal investigators allow.

Metzger: I think so. I think that was always something that impressed me about the NIH, was that there were no institutional or departmental barriers. Again, there may be barriers that are set up because of personality differences, but that is sort of idiosyncratic. In other words, I don't think the institution certainly fosters, has always fostered free exchange of people, resources, and so on.

Khot: You stated that when you came to the NIH in the late '50s, one of the trends developing at the time was the application of protein chemistry to immunology. How important of a factor did the fact that this was such a new field play in allowing researchers great flexibility in learning? Others have commented that because immunology or protein chemistry were so new, that there wasn't really any established ways of learning it, and so, like you said, there is, you know, your principal investigator was really doing

something else, and so protein chemistry as it applies to immunology was something that you wanted to know.

Metzger: Yes.

Khot: Do you think that because it was so new, that it was very important, too, and that allowed for the flexibility in how you learned it?

Metzger: Yes. I think to some extent that was true. It just wasn't a recognized discipline yet. There was something called immunochemistry, but that really had more to do with studying antigen-antibody interactions and not sort of protein chemistry per se. So, basically, one was, for many, many years during the growth of that area of immunology, one basically adopted the techniques that were being developed by the biochemists and applied them to proteins that were of interest to immunologists. There was no formal training in that sense.

Khot: Do you think that the way in which you learned how to study this field of inquiry laid the foundation for others to study the field?

Metzger: I'm not sure I understand the question.

Khot: It was such a new field at the time, and you learned it kind of in your own unique way. Do you feel like that, when you went on to teach the field or others came on to learn protein chemistry as it applies to immunology, do you think the way that you learned it really kind of set the foundation for how it was taught in the future?

Metzger: That's hard to say. Yeah. I'd find it hard to respond to that.

Khot: Okay. Do you recall if there was ever any specific research agenda for the

Associate Training Program scientists?

Metzger: No.

Khot: Who decided what research you would do? Is it something you decided?

Metzger: It was strictly on the basis of discussions with one's preceptor.

Khot: Okay.

Metzger: This is not to say that there weren't programs at the NIH that were a little bit more directed and where potentially individuals who were in training expected to work in certain specific directions. I think that varied, and I can't – I either don't remember or never knew particular examples that I could give you of that. But this, again, was one of the things that, particularly in the institute that I was in, it was more, when I say it sort of had a more academic ambience, it was also to some extent very heavily slanted towards basic research. And so, for example, the person with whom I was working, the principal investigator, was basically a protein chemist. That was his training. He was actually a physical chemist or a polymer chemist who got interested in studying proteins. We were in something called the clinical endocrinology branch, which was heavily oriented towards, almost exclusively oriented towards the thyroid and its diseases. So my preceptor, when he moved to the NIH, stopped working principally on pepsin, which he had been working on and done – I'm not sure exactly why he had chosen pepsin. Well, that's irrelevant. But, in any case, he stopped working exclusively on pepsin and more or less dropped that protein and started working on thyroglobulin because thyroglobulin is

related to the thyroid. But the kinds of questions that he was asking in his studies on thyroglobulin and that I became engaged in with him were very fundamental questions having to do with trying to understand protein structure, and so we were in a thyroid section, so we chose a protein that was relevant to the thyroid. But the questions we were asking were very generic questions.

Khot: Okay. What about the Associate Training Program most appealed to you?

Metzger: Well, it was a small program. It was considered to be a little bit of an elite program. It was a highly selected group. It included a substantial didactic component so that many of us whose premedical training had not been all that rigorous in terms of physical chemistry, mathematics, and so on, organic chemistry, had a chance to at least get some further training in those areas. It wasn't like getting a Ph.D., but at least one became familiar with a little bit more the approaches and methodologies, and so that didactic component was a very nice aspect to it. The other aspect of the Research Associate Program was that there was no service component to it whatsoever. The only thing that one was asked to do was to work hard and to get training, so, unlike the clinical associate program, where at least part of one's time one was performing a service function, although always in a training context, for the research associates, there was no aspect of that at all. So that seemed like a pretty good deal.

Khot: You had to devote all your time towards just research.

Metzger: Towards developing yourself, your own credentials.

Khot: Can you elaborate on how the style of your laboratory chief and clinical director during your training in the Associate Training Program influenced your style as a scientific instructor?

Metzger: Well, it certainly was an ambience or environment where the persuasiveness of one's arguments was basically all that counted, so it wasn't one's position or one's title or one's looks or anything else. It was basically whether you had a case to make, and so that was rigorous. It was congenial, on the other hand. And then, generally, people worked hard. We had a journal club, as far as I was a member, five days a week. People got together, had their lunch together very often, brown-bagged it and discussed science, so it was a very intensive but congenial atmosphere and people were, as I say, treated as equals based upon their knowledge and not upon their positions. That was very nice.

Khot: Do you think that most alumni from the program used the training they received at the time to train scientists in a novel way anyway?

Metzger: I don't know that it was particularly novel. I mean, the NIH at that time was a little bit novel in terms of – and I'm saying that even coming from Columbia, where at that time Columbia was probably, if not novel, at least a little bit unusual in the extent to which there was a very substantial interaction between researchers in the preclinical fields and clinical fields. I don't think there were probably all that many departments of medicine at that time, for example, that had Ph.D.'s as part of the medical faculty, which was true at Columbia. So there already was a very strong research

atmosphere in my medical school, and that was certainly also true at the NIH. And, in fact, there were a lot of interactions between the faculty at Yale and Hopkins and Columbia and schools like that and the NIH. That's where the NIH recruited a lot of people from, Duke and so on. So in that sense, this was part of a continuum, but it was certainly... I mean, the NIH was sort of the extreme in that trend.

Khot: You commented that much of the nostalgia for the ATP, the Associate Training Program, may be due to the fact that much of the intimacy when NIH was smaller is gone and that some of the things we talked about... knowing someone on their first-name basis, is not as evident. Can you elaborate on the atmosphere and how it's changed?

Metzger: Well, first of all, I think I'm not sure what question I was responding to there, whether you're quoting anybody, but that may have been a question relating to how other people felt nostalgic about it. I don't feel that nostalgic about it. It was a little bit different, but science was different, or biomedical science was different. Experiments were usually simpler, by and large. They weren't necessarily easier, but there were a lot less rules, and that doesn't mean to say that I'm sorry that there are rules now, because some of those rules are critical, whether it has to do with use of radioisotopes, use of animals, selecting people, mentoring people, etc., etc., etc., so there's certainly a lot more regulations than there were then. There is much more bureaucracy than there was then. And, again, I emphasize that I don't necessarily say it was better, therefore. It was just different. It

was less complicated. And research groups tended to be smaller, and, of course, the NIH community was smaller. There were more trees around, fewer buildings, and, of course, that always in some ways gives one a warmer feeling, a more intimate kind of feeling. Again, in my own case, I happened to have been in a branch that I think, even at that time, was a little bit unusual in the extent to which people within the department interacted socially. They were close friends, really. I think that's less true nowadays. It wasn't even that true at that time in many other groups, and I think maybe a little bit less true now.

Khot: How did your experience in SSU training program in the late '50s modify your career decisions?

Metzger: Well, before I even left here on the postdoctoral fellowship for another postdoctoral fellowship, I had already been offered a position here. At that time, one of the very nice situations at that time which made life simpler was that the NIH really, you either had a temporary two- or three- or four-year position or you had a permanent position and there was nothing in between, and so I was offered a position, and I accepted it. And so I didn't weigh a lot of different options, not because I couldn't have had other options, but I certainly enjoyed the Washington community, I enjoyed the NIH community, and because of family reasons, we wanted to come back to the East Coast, so in that sense it's hard to say how it influenced my decision. It was a very wonderful opportunity to be offered that, so I grabbed it.

Khot: But before you'd come here, you'd planned on returning back to, when you initially applied, you planned on coming here for a few years and going back to...

Metzger: Well, somewhere, yes.

Khot: Yeah, academic medicine.

Metzger: That's right. And without, at this point, looking for a job or, at that time – I'm not even sure how one would have looked for a job, but there was just no need to. Before I even got to that stage, I was offered a very nice position to set up my own laboratory in the institute in which I'd been trained, and it just seemed like a terrific deal.

Khot: Okay. Dr. Edward Rall has commented that the ATP, the Associate Training Program, had a major influence on medical education because of the addition of a serious research component to the training of M.D.s who were going to end up in universities was pioneered here. Would you elaborate on that? Do you agree with that?

Metzger: Well, he certainly is in a much better position now to say how true that was, but I think that was true. As I mentioned to you, particularly in the Research Associate Program, not only in the Research Associate Program, but there was, and still is, a sort of "graduate school" here that now is run through the Foundation for Advanced Education in the Sciences, and we were strongly encouraged to take courses there. So that encouragement and maybe availability of additional didactic training certainly was a very attractive component and I think did influence other programs and probably

was, if not unique, at least unusual in other training programs to the extent that they existed. So we had the didactic program. That was part of the Research Associate Program, intrinsically part of it, which was sort of required. There were the FAES courses, and then I even took some courses at Georgetown, at one of the local universities. So that kind of continued, encouragement of continued training was a very heavy component. But, of course, we also needed it more than perhaps some of the M.D.'s who are coming through now because I think at least some of the M.D.'s that came through later had a much more rigorous scientific training during their college years than some of us did.

Khot: Do you feel that the ATP has, if at all, changed the reputation of NIH?

Metzger: Oh, yes. I think – well, only in the sense that I think many of the academic leaders, certainly in my generation, had gone through the NIH program. I think, of course, on the basis of your prior statement, part of the success of the NIH program has been that it has been copied or at least used as the basis for providing similar kinds of programs at universities, and so to some extent, it no longer is unique. And that, of course, was one of the successes of the NIH program. So it may not, the NIH program per se, may not have as much influence on the new generation of academic leaders because there are other places where they can get that training.

Khot: In your opinion, what has been the long-term effect – you mentioned a little bit of this – of the ATP alumni on the academic world and scientific research?

Metzger: Well, I would say that one of the great strengths of the NIH biomedical, of the U.S. biomedical community, is the extent to which clinicians or clinically trained people, medically trained people, can do, can train themselves and are given the opportunity to get involved in fairly basic research, and where the interaction between basic researchers and clinicians is as close as it is. In many countries, that's simply not possible. If you are an M.D. and are in a clinical department, you simply don't have the ability to also get the support and the time to conduct more fundamental research. And I think the extent to which that is possible in the U.S. or has been possible in the U.S. certainly was contributed to by the intramural program. I think that may be changing, and the number of physicians who are doing, having that kind of combined career or who do what I did is changing and is decreasing so that there are some people who are concerned about that trend, and it's not clear – and there are many reasons, I think, why that trend is going on. But I think undoubtedly during that period of the '60s, '70s, '80s, the bedside-to-bench and bench-to-bedside kind of interactions certainly was very heavily influenced by the NIH intramural program.

Khot: Dr. Goldstein and Dr. Brown at Southwestern had written an article about the clinical investigator, and they talked about this, over a career, how the inspiration for patient-oriented research becomes translated into disease-oriented research later, or at least in their career and many of the others. And then I'd spoken with Dr. Schechter, and he talked about

sometimes what's difficult now is it's gotten so sophisticated that closing the loop is sometimes difficult, getting that translational research to apply back to the bedside. Over a career, sometimes that's not possible. Do you feel that, do you agree with that?

Metzger: Yes. I think that in some ways all research has become more complicated in the sense that there are more and more disciplines that need to be applied to do the kind of research that is now possible at all levels, whether it's at the basic level or at the clinical level or at some translational level, whatever. And so I think it's true at the fundamental level that, one, you find more and more authors on a paper because collaborations are necessary. No individual small group can do that. Now, in my own lab, I still try because that's the way I was trained and I've sort of almost deliberately tried to perform research where we don't have dozens of people or half a dozen people on a paper, so that it's me and a postdoc or me and two postdocs, or maybe one collaborator and a postdoc, and so on. But for a lot of research, that's just not possible. And so I think to some extent it's in the nature of – it's because the fields are advancing that one needs multiple inputs, and we don't have quite the number of co-authors as the NASA people do and so on, but sometimes you see papers with dozens of people, and it's the nature of the field.

Khot: Dr. Fauci described how the work he did with the inflammatory response and mitosis and the eventual cure came from that bench work-to-bedside phenomenon in the ATP. Can you describe any clinically-driven paradigm

shifts that came as a result of training in the program, either in your research or others', in which... I know you weren't directly seeing patients, but any clinical work you did earlier influence your subsequent research?

Metzger: Well, it's hard for me to give you a specific case in my own case, but there's no question that I've always valued my medical training as giving me sort of a sense of direction and perspective to my own work. And in immunology, of course, it's relatively easy making the clinical connections, so that even though I'm trying to ask some pretty fundamental questions in my own work, there are some very direct clinical applications, and, in point of fact, it's very easy for me to extrapolate how the kinds of questions that we're asking in the system that we're exploring have very direct implications for potential therapeutic approaches. That's generally true in immunology, so I think anybody who's an immunologist almost by definition is working in a clinically relevant area. It's that sort of a field.

Khot: Did the collaboration with other alumni from the program continue after you became a tenured intramural investigator?

Metzger: I don't think more so than with others necessarily.

Khot: It's been hypothesized that the ATP sort of created an "invisible college".

Metzger: No, I wouldn't say that that was necessarily true in my own case. First of all, there weren't all that many in my class of trainees. There weren't all that many people in immunology. The other thing I would say is that I'm not, if you have a whole spectrum of people, I'm not one who has done a lot of collaborative work to begin with other people. I tend to be a little bit

more of a loner in that sense. And so if I think about the other people who are, not postdoctoral but who are my peers in the sense of an equivalent level of seniority, I don't think the people who I've collaborated with tended to be people who had been at the NIH in the training program.

Khot: Could you discuss any unintended negative effects the program may have had in keeping women or minorities out of high-level research positions, as these groups were not represented in the program.

Metzger: Well, they were not represented, but I certainly never had the feeling that they were kept out in any way. If you just do the raw statistics... Well, at the time that I went to medical school, my medical school class, they still had quotas on women, and so only, I think, 10 percent of the students in my medical school class were women to begin with. Several of those were older women, actually, somewhat older women. They weren't old women, but they were older than perhaps the average. So since, as I mentioned, only 10 percent of the class in general went into academia, 10 percent of 10 percent is 1 percent, so I don't think there were very many women from my class that I can remember that went into research at all. Whether maybe they felt... Actually, I don't think at Columbia they certainly would have felt that research was not appropriate for women to do because the person who had the most influence on me in terms of going into research was a woman, so there were lots of, I would say at least – and I can only speak of Columbia, where I know about – there were plenty of women who were role models that were in research, including some who had combined careers of

clinical and pre-clinical sort of science research careers. There were heads of departments who were women – not many, but the head of surgical pathology was a woman; I think, I'm not sure, but maybe the head of, I'm not sure whether the head of anesthesiology, but Virginia Apgar, who was a major figure – you may have heard of the Apgar score – who was on a postage stamp. She was a woman at Columbia and was very highly regarded. But I do know that as a young researcher here at the NIH, it was many, many, many, many years, probably not until the late '70s, that we had any applicants who were women. So I don't have the feeling that there were a lot of applicants who were not admitted to the corps, so to speak. It's hard to know all of the sociological and other reasons why there were, in fact, many applicants.

Khot: Can you discuss the possibility today, in an atmosphere much more individualistic and less service oriented, for the government to mobilize medical talent as it did in the late '60s and early '70s for specific objectives, let's say, like the AIDS crisis in Africa. Do you think that would be a possibility today?

Metzger: Let me hear your introductory sentence again.

Khot: Can you discuss the possibility today, in an atmosphere that seems to be much more individualistic and less service oriented.

Metzger: Oh, I don't know that that's true. I know that's what they say. I'm not willing to accept that young people nowadays are any less service oriented. I don't have that feeling.

Khot: Do you feel it would be possible to mobilize medical talent?

Metzger: Oh, sure. I just don't know the statistics, but I'd be surprised if the people in the Peace Corps have more trouble recruiting young people – I don't know that that's true – than they did have. I think to some extent, as our politics has become a little bit more transparent, people are a little bit more realistic about the nature of the political establishment, perhaps, than we were, and so maybe aren't quite as naive. But I don't think people are less idealistic. I think that's every older generation claims that, and I just don't believe that. So I think, yes, I think if people became convinced that they could do, that they could be of assistance, they would do it. Now, let me give you an example. We had, when I came here, we had at the NIH a program that was sort of equivalent to a Head Start program where many of us taught black kids in a virtual ghetto community in Kensington, which is north of here. It was a volunteer program, and we'd spend an evening a week or every two weeks – I forget how often – to just teach, either tutoring young kids or even just reading to preschool kids. Well, I don't think there are a lot of people who are doing that sort of thing now.....there was complete discrimination and segregation. There are Head Start programs, and those just don't exist. So I think there are still a lot of people who are doing volunteer work. I think the younger generation has gotten a bad rap there, but I think that happens every generation.

Khot: Over the past few years, there's been a movement in our society to honor those who served in the armed forces during either World War II or

Vietnam War. On the other hand, while the legacy of Associate Training Program alumni has been enormous in altering American medicine, there's the recognition they're somewhat lacking, and there is still somewhat the negative connotation associated with the term "yellow beret". Are you aware of any sensitivity or resentment among associates?

Metzger:

No. And I don't think that's a real valid argument in the sense that I don't think many of us felt that coming to the NIH, that we came to the NIH other than altruistic or service-oriented kind of belief. You know, to some extent there are a lot of people for whom, either because they're in fortunate circumstances or because of philosophical reasons, feel that there are more important things than making the maximum amount of money. And clearly, people who go into, become teachers or go into academic work are not necessarily making as much money as they could if they wanted to focus on making more money. That's true of a lot of things, a lot of professions. So I don't think anybody who came here for that deserves special recognition for that reason. As far as comparing us to the military, that's a little bit different. It seems to me, in the military at least, there is the possibility that you're going to get hurt doing it, and that is a big sacrifice, and that was never a risk for us, so I don't think we should be treated, even though many of us were, I guess all of us except those who had a punctured eardrum or had some other medical problem, we were a uniformed service, but I don't think we were entitled to the kind of recognition that the people who were in the military.

Khot: We talked a little bit about the recognition for service versus the recognition for sacrifice. In the military, there's a tremendous amount of sacrifice.

Metzger: Potentially, sure, sure.

Khot: But yet the Associate Training Program, the amount of rewards of the service done by people who were in the program has now turned out, at least somewhat, has had a major impact on American society.

Metzger: Sure. But I don't, I think the people who should be honored should be the people who designed the program rather than the ones who were in it. I mean, all of us, I think, choose the way we conduct ourselves professionally for a combination of motivations. Some of them are self-serving; some of them may have an element of service to it. But I don't think that any of us felt that we were performing, that there was any great sacrifice to being in this program. Quite the opposite. It was a privilege. And we were paid relatively well compared to the rest of society, not necessarily... I don't know that we were paid less well. We may even have been paid better than people doing residencies, probably. So I don't think we felt that we were sacrificing anything.

Khot: I've just got a few more questions. In 1967, Representative Daniel Flood of the House Appropriations Subcommittee on Labor, Health and Education stated, "A quiet revolution in the practice of medicine is taking place as a direct result of research." Can you comment on that? One of the issues was that it has been somewhat of a quiet revolution initially in the '60s. Do you feel that still is the case today?

Metzger: I'm not sure what is being referred to.

Khot: His comment that this, what he calls a quiet revolution.

Metzger: Yes, but what do you think he was referring to there?

Khot: He's referring to biomedical research that was done at the NIH.

Metzger: Well, I mean, you may know the history of medicine better than I do, but my feeling, the recognition that careful, rigorous documentation analysis both of pathological material and applying chemistry and physiology and biochemistry and physics to medical problems, I think that has a long history that goes back to, well, you can go back certainly to the Renaissance, and I'm not sure that there was a revolution of the sort, of any sort philosophically. There certainly was a continuous acceleration, and I think that with the amount of funding that was applied to that, it certainly accelerated that thing. I mean, the idea that the laboratory bench had something to contribute to medical care and understanding that, I think, goes back a long time. And certainly in the history of teaching of medicine in the United States, I think that goes back to the '20s and '30s at least. And certainly the person who was chief of medicine where I was, at Columbia, that was totally his orientation after we received that training, and that came out of the Osler school and Hopkins and so on. So I think that goes back. I think what the acceleration that was promoted by the tremendous amount of funds that were applied to it certainly promoted that in an accelerated fashion, but I'm not sure that was sort of revolutionary. Maybe that's what he was talking about, the grants program in particular

and so on.

Khot: You mentioned this a little bit. In 1995, the NIH Director's Panel on Clinical Research found that there was low physician funding for clinical research. And it was due primarily to the fact that physicians just weren't applying in sufficient numbers for NIH awards. Why do you think this is? And what do you think the cost is of having fewer physicians leading clinical research?

Metzger: Well, in terms of the causes, I think they probably are multiple. I think that while there has been more funding, to some extent there is also more competition. How that balance has worked out, I just don't know. I mean, when I began in research, the opportunities for getting research support were accelerating very, very rapidly, and so those of us who were already enthusiastic about doing that had a pretty easy time. I mean, the idea that somebody could go from, after a year of internship and a year of residency and one and a half years of working in the laboratory and be offered a tenured position, a lifetime, virtually tenured position with a realistic outlook for not being rewarded munificently but at least getting a very livable salary and research support, that was just unheard of either before or after. I mean, now it's much, much tougher. You have to spend that many more years. And so there was that special period. Now, before then, I think one, the people who went into research either felt they had a calling, like a priest or something – I mean, it really was a sacrifice because the pay was awful, and it was very hard getting research support – or you had to be

independently wealthy, in which case – and that's always been true in science, that wealthy people could afford to sort of dabble in research, not using dabbling in a pejorative sense, but they didn't have to earn money doing it. So there were those kinds of people in research. And nowadays, I think, again, it requires either, it requires, in a sense, somewhat more sacrifice, I think, because the funding is less assured. There's more competition, there's more competition from people who have more direct training in the sciences than the M.D.'s. So for the M.D. who wants to pursue research, he or she has not only got to do all their clinical training and everything, but now there's a greater body of basic scientific training that they need to compete. So it's a tougher career path. I think that's one reason. I think to some extent, in all of the professions and so on, people expect a little bit more out of life than they did maybe 20, 30, or 40 years ago. Teachers expect to be rewarded better than they were rewarded 30 or 40 years ago, and so there is perhaps a tendency for bright people who have a choice of careers to move into careers that are rewarded a little bit more so they can live a somewhat better life. Then also, of course, there are changes in medical practice which make it more and more difficult, at the moment, for physicians to follow both types of career because of the pressures of the HMOs and so on. So I think that's new. How serious is this trend? I think we won't really know. I think many of us or many people certainly feel that the "physician scientist" plays a very special, if not unique, role in biomedical research. I'm not convinced that that's really true. It's easy to

say it's true, but I'm not sure that the data are really there. I think there are more and more scientifically trained people who are aware of medical problems, who one way or another, who sort of pick up their medical training in pretty such the sort of ad hoc way that we picked up our scientific training and who may be quite sophisticated and who may have some of the same perspectives that those of us who went the medical route into research went. So I'm not sure that we're losing a critical group of people. It's a different group of people, but I'm not sure that biomedical research is really being damaged by it. I think there's that possibility, but I'm not sure it's happening. The other thing that I feel very strongly is happening, but I tend to be a little bit of an optimist in that sense, is that I think this may be to some extent a temporary thing because at the moment the quickest way to make progress in disease-related research is to work at the molecular or fairly basic level, because with the genetics approach and so on, and the biochemical tools that are available, it's much easier doing animal research than it is doing clinical research, much easier doing test-tube research than it is doing animal research, or cell research is easier than doing animal research, and one can make tremendous progress in disease-related research. As soon as some of those things can be directed towards the bedside, there's going to be, I think, great excitement again about doing clinical research. And I think to an important extent, people go where the fun is, where the excitement is, and I think the excitement is going to go back to doing clinical research because people are going to want to apply.

And already I think that's true. They're going to want to apply the new genetics, the proteomics to clinical research. So I think that to some extent the whole thing is driven by enthusiasms and that, in fact, the young people who are opting to do laboratory research rather than clinical research, they're making the right choice because that's where the fun is. That's where the excitement is at the moment.

Khot: So you do think that the sense of excitement and unlimited possibility that used to be available in clinical medicine has really diminished.

Metzger: I think it's diminished somewhat, but I think it's a temporary thing. It's not that it's diminished; it's that something else is taking its place.

Khot: Okay.

Metzger: I think certainly from what I can see, at least working in a clinical branch, I mean, I'm working a branch, the young people have just as much interest in doing things that are relevant to human disease as they ever have.

Khot: Do you think that has been more influential than, let's say, the financial or career anxieties that physicians now face, the fact that basic science research or going into that has become more appealing over doing clinical research, is more of a draw than the financial and career anxieties are a deterrent?

Metzger: It's hard to know. You'd have to ask them. I don't know.

Khot: There's just like two more questions. In recent years, the concept of translational research has come to somewhat of a directional bias in which most basic discoveries are made in basic science labs and then applied to the

clinic. I think we've kind of talked about this a little bit. Is there anything else you wanted to add about that? Do you feel that the technology required to do biomedical research has become so sophisticated that training someone to do clinical research is hard because they can't really keep up with that sophistication?

Metzger: Well, I think it's more difficult, and as we've already said, it requires more collaborative efforts and so on. But, of course, it's also added to the excitement because one can get more answers, more definitive answers, more quickly. And so I think in that sense, while it may discourage certain people, I think others must also be encouraged by the kind of progress one is making, at least in terms of, not necessarily in doing something about these diseases – I think we're still at a pretty early stage – but certainly in learning about them. The amount of new knowledge, good, solid knowledge that one can depend on in all areas I would think would be very attractive to people.

Khot: The last question I have. I have a quote of yours, and I can show you in what context it was said. You were referring to the strategic planning that sometimes occurs at the NIH, and you said, "The idea that one can almost legislate progress and research is a very attractive idea, and it has some validity at the right time. But there are also very strong arguments against it, certainly against having a system that doesn't allow for people to follow their noses." Considering the unpredictable nature of scientific discovery, can you comment on how such – and this is my word – "institutionalizing"

of science at the NIH affected your research both when you came here originally and now.

Metzger: Well, I'm not sure. Picking up on your word, I'm not sure institutionalizing it, but directing it. I think, for example... Well, let me respond, first of all, directly to your question. I don't think it affected my work at all, and I have never felt any pressure from outside, either from the NIH administration or from my peer group or from the community at large, I've never particularly felt any pressure to direct my research in any way. And I don't know how many people are in a situation where they feel that sort of pressure and whether that's changed at all. I'm not sure it's changed all that much during my lifetime in biomedical research. I think there have always been instances or places where the research has been somewhat goal oriented in terms of finding a cure for a particular disease or of trying to understand the mechanisms of a particular disease. That's always been one theme in biomedical research, and the other theme has been just trying to understand biological systems with the idea that knowledge inevitably will have applications. I think allowing people to follow their noses in the sense of what is most interesting or what is most likely to be productive of interesting new knowledge, I think that also is a continuing trend, and I don't think, so far, there's been a serious undermining of that kind of support in the United States, at least. So when you have something like an AIDS crisis, I think it's perfectly appropriate for the United States government, through various techniques, to try and cajole, bribe, influence

people to try and work in that area, and sometimes cajoling and bribing and rewarding people who work in the area can speed up progress. If you get intelligent people to concentrate, if you get more intelligent people to concentrate on the particular problem, I think there is a greater likelihood that you'll find an answer more quickly. If, on the other hand, you overdo that and you don't leave enough right people to work in other areas, if you put too many blinders on them, then you may lose opportunities, and one can certainly just give innumerable examples of where unrelated research ultimately became very critical to what you were interested in. So it's a balance. And I think at the moment the balance in the U.S. is pretty good, and I think there's always going to be a little bit of an adversarial relationship between the public, as represented by the politicians, and the scientific community and I think that's healthy. I think the public... I mean, we are a – it is the National Institutes of Health. It's not the National Institute of Scholarly Knowledge. I think that's fine. I think, in the history of science, the connection of science and real problems, of applications, has been a very healthy one, and I don't think that we should forget that.

Khot: Dr. Metzger, thank you for allowing me the opportunity to conduct this interview.

Metzger: You're welcome.

Khot: Are there any other associates that you can think of that would be particularly good to speak with? I mean, we've spoken with a few here.

Metzger: You've spoken with Alan Schechter?

Khot: Yes.

End of Interview