

## Conversation with Enoch Gordis

In this occasional series we record the views and personal experience of people who have specially contributed to the evolution of ideas in the Journal's field of interest. After 15 years as director of an alcohol treatment program in New York City, Enoch Gordis was appointed director of the US National Institute on Alcohol Abuse and Alcoholism (NIAAA) in 1986. He has met that responsibility with outstanding success.

### STARTING OFF IN MEDICINE—AND MUSIC

*A: What I would like to do today is talk with you about your career and achieve an understanding of what has contributed to it—the influences on your personal career path.*

*EG:* I think there were influences on my choosing medicine as a career. Although there were no doctors in my immediate family, medicine was a highly respected profession. But as far as getting into the alcoholism world, there really were no family influences. There was no alcoholism that I knew of in my immediate family or in close relatives. I was raised in a fairly observant Jewish family. My father was a distinguished rabbi. Although the prevalence of alcoholism in Jews is said to be low, it is probably higher than people think. Nevertheless, it was a topic remote from the Jewish culture in which I grew up. I am not the only person with this kind of a background who ended up in the alcoholism world. There are distinguished clinicians in the United States and the United Kingdom with a similar background. But had you asked me in medical school whether I would be entering into this world, the answer would have been, 'I don't know what you're talking about'.

*A: You went to Columbia University and you are from New York originally.*

*EG:* New York City born and bred.

*A: When you entered college, what were you planning to do at that time?*

*EG:* I began, I believe—this is going back a while—as a pre-engineering student, but by the second year, I had changed my mind to premed and from then, I was on a pretty straight track into medical school.

*A: Because, in fact, you went directly from college to medical school?*

*EG:* Right. It was Columbia University: the college was wonderful and the medical school was good. I have no complaints. The education was fine.



Enoch Gordis

*A: And what area of medicine did you specialize in?*

*EG:* I ended up in internal medicine, but that is a function of the residency. In those days the choice of specialty was made towards the end of medical school, or even during internship. I think what has happened since is that young people have to make their mind up a lot sooner than we had to. Right now, it seems that students in their 3rd or 4th year of medical school already know what residency they will enter. I did not. But I had a great sympathy and interest for the basic sciences. I was young in medical school, and I think my skill with the clinical side came later than my ability to handle the basic sciences because clinical skills take a little bit of growing up, and I enjoyed the basic sciences very much.

*A: Any specially memorable teachers?*

*EG:* They had some real stars there—the use of radio-tracers in biology was a product of Columbia and there were some very distinguished people there—for example, Alfred Gilman, co-author of Goodman and Gilman's text

on pharmacology, was our pharmacology teacher—a very funny guy, besides being a wonderful teacher. So they had some very strong basic science. Of course, when we entered the clinical years, we had famous teachers such as Dr Robert Loeb, who was the Chair of the Department of Medicine, and there were others like him. I did not fully enjoy the clinical side of medicine until I was a few years older, when I began my residency. I needed a few more years, a little more seasoning and a little more confidence.

*A: And you maintained that interest in basic science throughout your career?*

*EG:* Yes. Actually, in the middle of my residency in internal medicine, which was at Mount Sinai Hospital in New York—I had interned at Mount Sinai also—I had a fellowship year in the laboratory of Drs Solomon Berson and Rosalyn Yalow at the Bronx Veterans Administration Hospital. That was the period just before they discovered the radioimmunoassay which revolutionized medicine and eventually won Roz the Nobel Prize. Sol had died of a heart attack before that—the prize is not awarded posthumously. Sol had taken a position as Chief of Medicine at Mount Sinai, which was a very demanding and difficult job, and aside from that he was a heavy smoker. I think he was 52 years old when he died. A brilliant guy—Roz is brilliant too, and they were extremely inventive, they worked very hard. Sol was an excellent violinist. Sol was very driven in all he did and we used to joke that he would play the ‘Minute Waltz’ in 56 s. During my year with them, I had the chance to see, first hand, the way great scientific minds operate. This was unforgettable.

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*A: Berson played the violin—did you share music with him?*

*EG:* Occasionally. Basically, I was a resident and his laboratory fellow, but music is a big part of my life, too, and was, in fact, for Sol, when he had free time. There was not much of it. On several occasions I visited him at his home when he would have people over and we would play together.

*A: What is your instrument?*

*EG:* Well, I play the piano pretty well and the cello badly. I have been playing the piano since I was five and I am still involved with it—not as much as I would like, but I am still involved. I play some chamber music occasionally. I took up the cello in my 30s and took lessons for 10 years to be of use to groups whose regular cellist did not show up. I did play string quartets for a few years but I have not played cello for several years now and one day I hope to get back to it.

## **WORKING WITH VINCENT DOLE AT ROCKEFELLER**

*A: And after your fellowship.*

*EG:* Well, I finished my residency at Mount Sinai after that year. First, I spent 6 months on the chest service. Mount Sinai had some great, great clinicians. and then finally, a year as Chief Resident in Medicine. I then wanted to go back to research. Sol Berson was friends with Vincent Dole who was Professor at the Rockefeller University. He made the connection—introduced me to Vince—and that led to a 10-year stay at the Rockefeller University laboratories with Vince.

*A: What did you do when you were at Rockefeller?*

*EG:* Like most people who come into an established program, I joined in the work of that laboratory, headed by Vince Dole, who was distinguished for his work in fat metabolism. Dr Dole had made important contributions before that in other areas—some related to fat metabolism, others not. For example, he was a pioneer in the theory of electrophoresis, but he had also done important work, in the decade prior to the time that I was with him, in obesity. He was one of the creators of the total liquid formulation diet for studying metabolism. He is often not given sufficient credit for that. He discovered the fundamental metabolic role of the non-esterified fatty acids, sometimes called free fatty acids, and their relation to glucose metabolism. There were others who contributed to that subject as well, but he was probably the first.

*A: So the focus in Dole’s laboratory when you arrived?*

*EG:* When I arrived in 1961, the laboratory was very much engaged in the metabolism of lipids and I was drawn into that. So was Edwin Bierman, who later became very distinguished in this field. I worked on the metabolism of chylomicrons and the exchange of fatty acids and triglycerides in tissue. Technology really generated a lot of the progress in the field in those days because, in the late 1950s, gas chromatography arrived as well as column- and thin-layer chromatography with silicic acid. Many of the applications of these technologies were pioneered at Rockefeller by Dole, Ahrens, Hirsch and others. So the field was ripe for the major advances in lipid metabolism which occurred in the 1960s, not only at the Rockefeller but in many places around the world.

*A: Give us an idea of what that technology could actually do?*

*EG:* This new technology—the ability to separate with very high resolution molecules whose separation was undreamt of in the previous era of bulk extraction—revolutionized the field. So, I entered at a very nice time and was able to do some work with turnover of individual triglycerides, and devised a method of separating chylomicrons for metabolic study. But then there was a slight shift in my interest. I had never forgotten the tragic death

at Mount Sinai of a teenage boy who died of carbon tetrachloride poisoning after cleaning his prized bicycle with that solvent. I spent a couple of years on carbon tetrachloride intoxication and I was one of the people contributing to the demonstration that free radicals are involved in carbon tetrachloride toxicity. I showed that fatty acids with trichloromethyl side chains were formed during carbon tetrachloride poisoning—they could have formed only by free radical mechanisms.

## THE METHADONE STORY

*A: When did Dole begin to get interested in addiction?*

*EG:* But at the same time, Vince Dole and colleagues became interested in addiction—this must have been around 1962. How that happened was one of the unpredictable events that shape history. While the laboratory was cranking along in fat metabolism, Vince Dole agreed to substitute one night for a member of a committee that New York City had established to look into the heroin problem. What struck him was that everybody had opinions but nobody had any evidence, a very disturbing state of affairs for a scientist. So he decided to look into the heroin issue from scratch, with no biases. The way to do that at Rockefeller was to admit some heroin addicts into the hospital and study them on Rockefeller's clinical research unit, which was world famous. Now, you should understand that the Rockefeller University is not a place you usually associate with 'junkies'. Much more than now, it had a kind of lace doily quality to its social aspects. For example, there was a faculty dining room where only the faculty and their guests ate. Waitresses in tidy aprons would serve you. One good thing about that—disregarding its elitism—was that you could make lunch dates with people from other laboratories, and sit down quietly and exchange ideas in a friendly and unofficial way about scientific issues. That was lost when the big cafeteria and its democratic style replaced the dining room. But I guess there is a trade-off for everything! Anyhow, you have to understand that Rockefeller was a very elegant place—well-manicured lawns, wood-paneled libraries, tennis court and an understated, slightly aristocratic style. So the idea of bringing heroin addicts into the sacred halls of Rockefeller was novel.

*A: And controversial, I suspect.*

*EG:* Yes, it was. But Vince Dole went right to the top. He went to the President of the University, who at that time was Dr Detlev Bronk. As soon as Vince told him what he wanted to do, Bronk said, 'I think you ought to do it', and that was that. To some, Vince was tarnishing his reputation by studying such an unimportant topic. Here was a man who was a master of mathematics, of theoretical

physical chemistry, who had made major contributions to metabolism and now he was going to study these terrible people in the Rockefeller University Hospital, and I must say that although it was never rude or loud, there was an undercurrent of derision for the scientific direction which Vince had chosen. Never explicit, but you could sense it. To some people, he had taken an inexplicable turn for the worse. But the hospital set up a special locked unit for the studies and the heroin addicts were studied there.

*A: Marie Nyswander was around at that time?*

*EG:* At that time, Marie Nyswander joined him from Lexington. She had a lot of clinical experience and had written very perceptively about the disease concept of addiction. She knew the patients intimately and was a brilliant psychiatrist who later became Vince's wife. But she was also his scientific partner. Mary Jeanne Kreek was a very talented young physician in the laboratory during that period. She had come from her residency years in Cornell- New York Hospital, and she was part of the early addiction studies. I was not, really, except as an observer. I did do some work on the analytical chemistry of methadone and gas chromatographic separation of drug stereoisomers. There were some great moments: I will tell you one of them. They tried out different drugs to see what the reaction of the addicts would be. When these patients were on the ward, their conversation was dominated by concerns about the next dose of heroin. and so different drugs were tried to see what would happen to this obsession. It was clear that heroin itself was not a promising drug because of the need for intravenous injection and the fact that it was short-lived, so the addict swung between the extremes of euphoria and distress several times each day.

*A: I can guess what comes next . . .*

*EG:* But then they tried methadone, which was a well-known opiate. It had been synthesized by the Germans during World War II. It was a narcotic like any other, except that it had two virtues. It was active orally, and its effects lasted a long time. Its detailed pharmacology was really not known. That was developed later by Mary Jeanne Kreek, when she developed assay methods, but its clinical use as an analgesic was known. They started giving methadone in increasing doses as the patients became tolerant to it. Remarkably, the patients' conversation shifted from drugs to ordinary topics such as work, school, sports. The wide swings between euphoria and distress ended. On one of the great days, I think, in medical history in the 1960s—in fact, maybe even in the whole century—Vince, Marie and Mary Jeanne discovered that patients on methadone could not distinguish intravenous heroin from saline. It was as if nature had briefly opened the curtain. That was the so-called blockading dose of methadone. Then, of course, from

then on, everything really began to cook. Some of those original six patients went on to see their lives turned around. Methadone maintenance treatment spread. Within a few years, Vince had a data base of thousands of patients in New York City in his own office. He knew the importance of data collection right from the start and he set up this computerized data base. There are some other great chapters in this story—for example, his work in the ‘Tombs’—then a notorious prison in New York—where he set up a methadone program. For six months, he visited the prison every day, dispensed methadone to the prisoners, eventually writing a paper in the *New England Journal of Medicine* that showed that the reincarceration rate after discharge was far lower in the patients continued on methadone.

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*A: Vince was an important influence on your professional life?*

*EG: Of course, Vince had a very great influence on me. He and Sol Berson were the two greatest scientists I have had the privilege to work with. I ask myself, what is it about them that makes them so special, because in the company of bright people, these two still stood out. There are several things. First of all, they managed to see a lead immediately—they could smell it. The second thing is that they never let the technology dictate the question. The question dictated what technology was needed. So if they had to learn a new technology to answer the question, and if the technology was available, they learned it. And the third thing, which is very striking about both of them, they always saw what the essential question was. They did not get bogged down in the trivia. I used to liken it—when I thought about it in the old days—to Bobby Fisher when he was chess champion of the world, making one of those moves which was so beautiful and, in retrospect, so obvious. But if it was so obvious, why did anybody else not think of it? It was that kind of genius that characterized both Sol and Vince. It is science operating at the very highest levels. I could never perform at a level anywhere near that. But at least, I learned what the ideal was, to be able to see these things.*

### **RUTH FOX AND THE START OF A PROFESSIONAL INTEREST IN ALCOHOLISM**

*A: How did you move into the study of addiction while you were at Rockefeller?*

*EG: There came a point in my career, in the 1960s, when the carbon tetrachloride work came to a stopping point. It could have been pursued. But by that time, the whole ambience of the laboratory was in the addiction world. So I said to myself, ‘You know, in 24 h a day, you might as well work on a big problem instead of a small one.’ Alcoholism was not yet a topic in that laboratory. So Marie introduced me to Ruth Fox, whom she had long known because they had had some of their psychiatric training together. Ruth Fox was a distinguished psychiatrist who had been interested in alcoholism for a long time. She had discarded psychoanalysis as alcoholism treatment because she found that the patients lying on the couch derived great insight but stayed drunk. She had an office on Manhattan’s east side and she brought AA into her office. She did other things also—psychodrama and LSD, a little craziness there once in a while, some of which would not stand the test of human subjects committees these days. In any case, she was a wonderful writer, a very charming person, and indefatigable. She also brought Antabuse over from Denmark—it had been introduced in 1949, so it was only about 15 years old—and she treated about 3000 patients in her own office with Antabuse. Marie had fixed me up with Ruth because I wanted to learn something about alcoholism while beginning some laboratory work. So I spent, I think, two mornings or a day or two a week with Ruth during my last couple of years at Rockefeller, in her office, watching how she handled the patients, talking to them and managing them. There were some funny episodes but I learned a hell of a lot from her. Ruth was not really a scientist herself but she respected science highly. She was one of the people responsible for the formation of the science committee of the New York Medical Society of Alcoholism, and these early groups were the forerunners of what later became The American Medical Society on Alcoholism and the Research Society on Alcoholism. Ruth was one of the people most responsible for bringing alcoholism into the mainstream of medical concerns.*

*A: When you talk about both Marie Nyswander and Ruth Fox, the idea of really talking with patients and treating them as a way to understand what the essential questions are, is apparent.*

### **PATIENTS CAN MAKE THE HYPOTHESES**

*EG: That’s right. Vince, in his tributes to Marie, who died a several years ago, often talked about how she emphasized the importance of listening to the patients because that is where the truth lay. And, of course, in medical school, we all learned this aphorism—listen to the patient*

—he is telling you the diagnosis. Well, from the scientific point of view, you listen to the patient and he is telling you the hypothesis. Marie emphasized that to Vince. She also had private patients in New York, some very distinguished people from the arts and literature who were treated with methadone. Vince, Marie, and colleagues such as Bob Newman, established major treatment programs at Beth Israel Hospital in New York. So yes, you are absolutely right, the issue of the patients is very important. That is why it still governs much of my thinking, even now, although I have been away from direct patient care for quite a while.

**'Well, from the scientific point of view, you listen to the patient and he is telling you the hypothesis.'**

*A: I know you ran a treatment program for many years and must have had the opportunity to listen to many patients.*

*EG: Yes. I left Rockefeller in 1971 and had an opportunity to establish and direct an alcoholism treatment program at the City Hospital at Elmhurst, one of the affiliated hospitals with the Mount Sinai School of Medicine. This program was in Queens, one of the other boroughs in New York City. During the next 14–15 years I was responsible for the care of almost 15 000 patients and I must have seen several thousand myself. I worked the clinic 3 days a week and made detox rounds and taught residents and met with the half-way house residents once or twice a week and took them on an outdoor hike every year, and so I have seen a lot of patients and talked to a lot of them.*

*A: Is the 'craving issue' perhaps an example of where clinicians need to listen to patients?*

*EG: The 'craving issue' has been difficult to operationalize for research but clinicians find it obvious and real. Able scientists have been trying to define it and measure it, and there has been some success, especially with new interview instruments derived from the experience with obsessive-compulsive disease (Anton *et al.* 1996). But even now, people have different ways of looking at what craving is. The question is, how do you translate this terrible sense of deprivation you see in the patients and their discomfort when they do not have the alcohol? How do you translate it into something which is interpretable physiologically and biochemically, and even experimentally?*

*A: OK, how do you do that?*

*EG: We talk a lot about dopamine, reward and the mesolimbic system and all that is very good—obviously, very apt. This system is not specific for any drug. The system seems to be involved with many other activities that are necessary to promote life so nature made them enjoyable, such as eating and sex. Also it seems to be more important in the anticipatory stage of drug use than in the consummatory phase. But unless you define*

*the boundaries of reward very widely, when I see someone who has been drinking a quart of vodka a day and cannot get along without it, and then he finally relapses, I do not see this drinking to be rewarding in any conventional sense. I think it is more like what Robinson and Berridge say about wanting but not necessarily liking (Robinson & Berridge 1993). There is a terrible sense of deprivation—that is a persistent impression from my clinical days—having seen so many patients. They are not drinking to get high anymore. They are drinking to relieve a profound dysphoria, one we still do not understand. That is my view. Others will disagree with it. But that is what I am left with after seeing so many patients. Abstinence in the alcoholic is akin to the feelings of a formerly 300-pound patient who has been reduced to 180 pounds and is always hungry. Our new medications are beginning to change that, and new research on the 'alcohol deprivation effect' is beginning to address this.*

#### **A CLINICAL DIRECTOR WITH NO TIME FOR BANALITIES**

*A: You had been trained in basic science and then were the Director of the Alcoholism Treatments Program for 14–15 years.*

*EG: I had been trained in basic sciences and knew my way around the laboratory and understood the scientific literature. I respected the fact that unless science was the foundation of treatment and policy we were going to be in trouble. That was one of the problems in our field. We had many slogans but very little science—especially on the treatment end. I would often be surprised to find that the whole agenda of an alcoholism meeting was to trumpet some banality such as 'alcoholism is a family disease' as if we had a monopoly on that! That is like discovering the sunrise. So one of the things I tried to do during my time with the program at Elmhurst Hospital was to try to teach, even at the bedside, the same way other faculty taught nephrology or gastroenterology. That is, you attended to the patient's needs, but you used the opportunity to talk to residents about the science that we had—whether it was tolerance or medical consequences or the nature of withdrawal. You told what the neuroscience or the genetics might be, even in those days, which were in the 1970s and early 1980s.*

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*A: A bit more about how you taught your residents . . .*

*EG: Research is much further along now but there was much good research in the 1970s and what I did*

with the residents was to prepare, with my colleagues, loose-leaf books with the most up-to-date reprints of articles from 12 or 13 different domains, which very much paralleled the domains we have in the Institute now. We would meet with the residents for tutorials two or three times a week, aside from the bedside care, and the resident was expected to prepare for it and read. We tried to make the month as educational as possible based on science, even though the main job was taking care of patients. We had a 20-bed detox unit in those days—a disappearing phenomenon. We had an outpatient clinic that met days and several evenings a week to accommodate working folks. We had a halfway house with a no-nonsense program. You had to pay rent to stay there, get a job or report on your interviews for jobs. You had to attend AA meetings, take Antabuse daily under observation, and get your life in order. I would like to say that the program was a great success, but it was not. Patients appeared to be ready for an independent sober life, but if you look at the ‘survival’ curves we published (‘survival’ to drinking) (Dwoskin *et al.* 1979) you see that within 3 or 4 months after discharge almost all the patients had relapsed. This told me that we were not there yet—we had a lot to learn.

*A: What else did your clinical program offer?*

*EG:* Our alcoholism program offered a whole range of specialties. We had neurology and psychiatry there within the program. We had a whole range of social services, plus a very large and able group of counselors who were mostly recovered, almost all recovered through AA. Near the end of my stay there, there were a few who were not. The evidence now shows that that is not essential for being a good counselor. There are aspects of personality and style which are more important than having been in recovery. But I remember, when we first started the program, I differed from Vince. When he began the methadone programs in New York in the early 1960s, he developed a cadre of successful former addicts to be counselors, and he did not have much use for social workers. When I came to Elmhurst Hospital, I had inherited that bias from Vince. However, the Social Work Department insisted—when we were mapping the new program—that counselors should come under their aegis, because they had to learn how to talk to a patient in a professional way, how to write a clear clinical note and how to keep records. I worried that once the counselors got their white coat on from the social work department, they would lose their AA fire. It turned out that the social workers were right. The counselors lost none of their AA fire. At the same time, they learned how to operate professionally. The program ran very well and was recognized as having very high standards for its day.

## **TAKING ON THE DIRECTORSHIP OF THE NATIONAL INSTITUTE ON ALCOHOL AND ALCOHOL ABUSE (NIAAA)**

*A: So the reason you were sought out as a candidate for the Institute Director was because of your commitment to science as the basis for our field, and you ran a program that was well respected.*

*EG:* I think that helped. The actual sequence was an accident, like so many things in life. But I also had a sense of what the political pressures and financial pressures were on programs. One day I would be teaching the residents something about tolerance, the next day I would be in front of City Hall with a billboard, demanding more money for treatment.

*A: And by then you certainly had a sense of the constituency?*

*EG:* At the time I came to NIAAA, I think it was extremely important to have a sense of the constituency, and what the impediments were. There were real problems faced by the treatment community—skepticism about treatment results, ambivalence in the public about whether alcoholism was a disease or a sin, problems with money. Treatment program directors used to meet every month. In the early 1970s treatment budgets were pretty good in New York, and we talked about treatment and science. As the economic woes started descending on the State, all sorts of problems arose with Albany and New York City. I would go home on Friday night after one of these meetings, morose and disheartened. On the other hand, sometimes the treatment field was its own worst enemy—by taking an antiscience approach, as if AA had all the answers in 1935 and there was nothing more to learn. Outcome data was seen as unnecessary. The idea of carrying out research on patients, to many of the old-timers, was anathema. But I can tell you, much depends on the leader of a particular treatment program. In my program, we had all the AA enthusiasm in the counselors that we needed and still were able to talk about research and do some small clinical studies. If the director really wants to do that and shows that he respects the traditions, at least what is valuable in them, and at the same time really wants to bring in a higher quality of self inspection and treatment outcome research, it can be done, and we did it.

*A: So what was for you the route to NIAAA?*

*EG:* The actual route to my being chosen to head NIAAA was just an accident—like many things in life that are important. I guess it was because of Charles Lieber [Dr Charles Lieber, an eminent scientist, Professor of Medicine at the Mount Sinai School of Medicine]. The position was vacant—my predecessor, Bob Niven, had retired. There was an able acting Director, Loran Archer, who had filled that role on several occasions during the

previous decade. Charlie Lieber called me at my office in Queens, New York and said, 'You know, the NIAAA Director position is open' and 'do you know anybody who might be interested?' I mentioned a few people—good people. and he said, 'How about you?' I said, 'No, I'm perfectly happy here. What do I want this for?' So he says, 'Well, think about it.' So, I called my brother, Leon, for advice. He is a very distinguished epidemiologist and at that time was Chairman of the Department at Johns Hopkins, and very savvy about academe and politics. He said to me, 'It's a good idea to go through a search because you can see what it's like. Then when there's a job that you really want, you will know what to expect.' So I called Charlie and said, 'OK, I'll apply.' I was not surprised by the interview because the night before the interview I sat down with my computer and I said to myself, 'What would I ask if I were on the search committee?' and listed the questions. They asked everything I had thought of. What is nice about it is, when you're interviewing for a job that you do not care if you get or not, you can say what you think. That always works well. It was a very able search committee, from the basic sciences, government, and from the treatment world, some of whom I knew very well. Others I did not, and I discussed the kinds of things we have been talking about, that we have to substitute science for the slogans. They asked me what were the biggest problems in our field. Of course, our biggest problem has not changed: we did not have a lay constituency for research, and 14 or 15 years later we still do not. It's better now, but we do not have a group supporting us like the American Heart Association, the Leukemia Society, the March of Dimes, or the Cystic Fibrosis Foundation.

**'The actual route to my being chosen to head NIAAA was just an accident—like many things in life that are important.'**

*A: You got onto the short list?*

*EG:* So the search committee considered me an attractive candidate and I ended up on the short list. At that point, the competitive juices started to flow. Up to then, I really did not care. The final decision was made by Dr Donald Ian Macdonald, then administrator of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) in which NIAAA was then located. I was chosen and I was very pleased because the other candidates were excellent people, any one of whom would have made a great Institute Director, and I have loved it. No job is all paradise, but the intellectual core of the work here is super. The science is interesting on every front. The chance to advance the field in a public way is also very good. I love working with the marvelous staff. It is a pleasure to come in here and be around such able people and to laugh

about things together, and finally, at the NIH (National Institutes of Health) there is a wonderful crowd of very smart people in different fields and it is an exciting place to be. Every job has the kind of drudge work that is necessary to keep the fires going. There is no such thing as total paradise, but the core of the work is terrific.

## **NIAAA AND THE SETTING OF OBJECTIVES**

*A: You have now been the Institute Director for 15 years?*

*EG:* October, 2001, was 15 years.

*A: In those 15 years, what were the objectives in the beginning for you and transitions after that?*

*EG:* When I came our institute was still in ADAMHA, not NIH (National Institutes of Health). We moved into the NIH in 1992, and originally the Institute had science as only one of its components with its meager budget. We also funded treatment programs and demonstrations. Things were changing. The Institute became much more science-oriented. But the biggest change—and that was mostly in the first years—was to change the whole image of what the field was about—that it was a field, like any other area of medicine, that it had to be science-based, that we had to stop living on slogans. The treatment community would have to be persuaded, and there were many people there who were ready to be persuaded, that the separation of the science from the treatment community had to end. There was an abyss between the two that was destructive because we needed each other. Treatment without science is witchcraft, and science without an arena to test its conclusions is irrelevant. So we needed each other and we had to get together, but we had to stop talking nonsense. We had to stop claiming rates of treatment success for which there was not the slightest shred of evidence. We had to make a better effort on the research side to communicate what we are finding, and if not its actual, its potential importance. because we did not have much actual information to tell them yet. Staking out those goals in the beginning, and sometimes quite explicitly, was probably the most serious change. Not that Bob Niven had not done a lot of that already. He had. But I think I gave it an extra jolt, which was important.

*A: From then on?*

*EG:* Once that got moving, things became more orderly. Nowadays we have large controlled clinical trials on one hand, major findings in human and animal genetics, neuroscience and toxicology on the other. Prevention became based on comparison trials—maybe not blinded—but they were brought into an area of respectable science. and we had some major conceptual advances in the field in the last 20 years. I do not claim

that I am responsible for them because Bob Niven did a lot before me. But I think I can say that the efforts of the Institute have been productive in many areas. Without very, very able people around me, nothing would have happened. However, I think that one job of Institute Director is to choose directions. Maybe thinking of a few himself, or herself, but also getting suggestions from outside and then choosing among them. We had some major decisions to make. For example, were we going to spend a lot of money on a large collaborative study of the genetics of alcoholism? We decided to do that, and we know now that it was a wise decision. We did not decide that single-handedly. In 1987, we had an important meeting. We invited genetics experts from outside the alcoholism field as well, and they almost all agreed that the time was right to do it. There were some naysayers. They felt that the adoption studies had some weaknesses. But the overwhelming consensus was that there was a significant genetic component to the vulnerability to alcoholism and that we should find the genes. Advances in neuroscience, of course, were dependent, in part, on the advances in technology: imaging, single cell recording, multielectrode recording, patch clamps, microdialysis, neurochemistry, and sophisticated cognitive testing.

So its been an exciting time. The more difficult obstacles have not been to get the science going, because, after all, what we do in science derives from advances made in other fields as well. Getting science to be recognized as an indispensable component of advances in our field by the whole community—that has been the biggest obstacle, and I think we have made some gains. Not utopia, but I think we have made some gains.

## THE REPUTATION OF ADDICTION SCIENCE

*A: Earlier, you talked about Vincent Dole being sort of stigmatized in a way by his shift into drug addiction.*

*EG: Yes, but that disappeared with time. He is now universally honored at home and abroad. He has received many awards, including the prestigious Lasker award.*

*A: Do you feel as if research on addictions is now perceived as more mainstream by the larger community of researchers?*

*EG: Yes, it definitely is becoming more mainstream. You can see it in all sorts of ways. You see questions on addiction on the boards of Internal Medicine. There is a psychiatry subsection on addiction. Addiction research makes the science columns of the popular press and the electronic media. So there is no question, it is radically different than it was 15 or 20 years ago. Still and all, I think that if, for example, you want to do molecular biology of addiction, drugs, or alcohol—some people in the universities*

*might tell you to choose some other route for your future. But it is certainly not the same death trap that it might have been viewed as by the academic world 20 years ago. There are private citizens nowadays who have donated money to establish alcohol research components at universities—for example, at the University of California in San Francisco, at the University of Texas in Austin and at the University of North Carolina. There are laypeople now who are willing to make a very public commitment to the idea that science is fundamental to progress in treatment.*

*A: One thing that I have heard about you is that you are incredibly well read about the different aspects of this field.*

*EG: Well, I try to keep up. It is difficult because, sometimes, one's reading time is taken up with the administrative side of work—there is a meeting here or some response to Congress there, or something from the Directorship of NIH which has to be responded to and a lot of requests to speak at meetings of different organizations or to the media. Sometimes one has to respond to all these things quickly, but I try to keep up.*

*A: The other thing that I have noticed is that, at the meetings, you also, as an Institute Director, talk to almost everyone about their research that is being presented.*

*EG: 'Everyone' is an exaggeration.*

*A: Even-handedly.*

*EG: I think there is more to it. You asked me what my family influences were. Here is one. The Talmud says at one point, 'Who is wise? He who learns from every man,' and it is funny that my attitude has been shaped by that. I believe that the best people in every discipline in our research world have important things to tell us, and then we have the issue of what can help to relieve the problems caused by alcohol now. The psychosocial research, especially prevention research, tends to be expensive, fuzzier, not as crisp as doing a study on some changes in neurochemistry. However, the fact is that rational social policy which follows from the application of science-based interventions—for example—legal alcohol levels for driving, minimum age for drinking—has already saved thousands of lives. We cannot make that claim yet for either genetics or neuroscience. The benefits of genetics and neuroscience are largely for the future. Yes, there are useful new medications for treatment which are products of neuroscience as well as clinical observation, but they are only moderately effective and more potent medications will come. So I think it is a big mistake to have a bias that one area of science or another is not valuable. Now obviously, when one is faced with choices and finite funds, one has to judge which direction is being productive and which is not. We may not need the 20th study on some well-mined topic in basic science any more than we might need another expensive study in some psychosocial area.*



Choices are necessary. But my view that we have valuable things to learn from the best people in all disciplines has paid off. It is funny that this attitude derives from my childhood. Some of these things leave a mark.

**‘The Talmud says at one point, “Who is wise? He who learns from every man,” and it is funny that my attitude has been shaped by that.’**

*A: You told me about the two major people who influenced on your life from a scientific perspective. But are there other colleagues that you felt you valued their input particularly?*

*EG: I’ve had many colleagues in the United States and elsewhere from whom I have learned a lot over the years. The problem in answering more specifically is that Berson, Yalow and Dole were part of my life when I was young and their stature and international reputation was unique. I am fortunate to have learned much from many splendid contemporary colleagues, but I would not want to risk omitting any of them by listing names.*

## LOOKING TOWARDS THE FUTURE

*A: Where do you see the future of the Institute? Or your career at this point?*

*EG: Well, I am 70 years old. Some people want to die at NIH if they are there, but I am not sure I am one of them. I have many interests. I might want to have a few years to pursue them again—whether it is grandchildren, music, the outdoors, and several others. Not that I want to give up thinking about this field. One aspect of my job is that I do not have enough unpressured thinking time. I gave a talk recently which I wanted to turn out well, so, being the director, I had the luxury of telling people for a few days, ‘please don’t bother me’, but that could not last very long. My career is not an issue any more. Sooner or later it will end, I do not know when, but it will not be forever. If you are asking what the future of the Institute is, I think we have terrific people out there now, any one of whom would make a splendid Institute Director. I think that the people who are not MDs, the PhDs, have become very sensitive in the last 10 years to the constituency issues which I mentioned before. Not all, but the more mature, seasoned ones. I think it will still be important to understand the politics of this field as well as the science. The ideological gaps still have to be overcome, and they are beginning to be overcome. I am happy to say that there are people both with MD degrees and PhD degrees who have that kind of insight these days and that probably was not true 20 years ago.*

*A: These days would someone’s degree be important in determining whether they could be Director?*

*EG: I do not think one would have to preclude anybody on account of their degree from being Institute Director.*

As far as the administrative side of NIAAA, we are doing well at NIH. One hears talk about institute mergers, even on a global scale. For example, collapsing the NIH into a few mega-institutes as suggested by Dr Varmus, the former NIH director. The issue of merging us with NIDA (the National Institute on Drug Abuse) perennially bubbles up. I am opposed to this for several reasons, and I believe that NIAAA will survive intact and flourish.

## THE NEED TO DEVELOP A LAY CONSTITUENCY

*A: You have mentioned that you think one of the most important things is that we need to develop a lay constituency for alcoholism research. Do you think that is going to be accomplished in the next 10 years?*

*EG: Constituency groups for other diseases have generally been formed by the families of the afflicted. They demand more research to help cure their loved ones, and they are vocal in Congress, and in the media. They have become powerful political forces, and some of these groups have themselves supported research in their areas apart from the NIH. The alcoholism field has no such organized constituency. I see several obstacles that we must overcome before we will have such a constituency. The first obstacle is the stigma attached to the diagnosis of alcoholism. Many people are ambivalent about alcoholism—they may believe it is a disease, but at the same time consider it a matter of defective character. Alcoholics are difficult to live with. Relatives of alcoholics are still not prepared to act together to demand more money for research—they are still embarrassed to admit that the condition exists in their families. Can this change? Yes, it can. Fred Goodwin, former director of the National Institute of Mental Health (NIMH) pointed out that advances in science remove stigma. Years ago, when someone died of cancer, the newspaper obituary would say he died ‘after a long illness’. Nowadays, the obituary will say, ‘she died of breast cancer’. This change has happened because science has brought new treatments, and most importantly, new hope for cancer patients. This will happen with us, too, and it is beginning.*

*A: Other obstacles?*

*EG: Another obstacle to developing a constituency for alcohol research is that the enormity of the alcohol problem is not noted by the public the way it notices the ‘war on drugs’. Alcohol problems cost more and kill more than all the illegal drugs combined, and the drug most likely to kill your teenager is alcohol. The beverage industry often likes to imply that this is not so. Parents of a drinking teenager will still say, ‘at least he’s not on drugs’. The media give this matter scant attention, perhaps*

because of their large alcohol advertising revenue. But this is beginning to change, partly as a result of some imaginative efforts by our institute, certain organizations such as 'MADD' (Mothers Against Drunk Driving) and partly because the science is now so intriguing and promising.

'Parents of a drinking teenager will still say, "at least he's not on drugs".'

## **VOLITION IS AN IDEA THAT MUCH NEEDS CLARIFICATION**

*A: Any other details?*

*EG:* A final obstacle to developing a lay constituency is intellectual. There are subtle issues within the 'disease concept of alcoholism' to which our field probably has not devoted enough attention. I define alcoholism as a persistent pathological appetite for alcohol—a pathological motivational state. But even if one accepts that, the issue of volition presents ambiguities that the public senses even if it cannot articulate them. Our own thinking has to be clear for the public to be convinced.

*A: So what do you personally make of the volition question?*

*EG:* The issue of volition is really a difficult one. Even for an alcoholic, the raising of bottle to lips is, in some ways, a voluntary act. He uses 'voluntary' musculature. He makes some decision and acts on it. So drinking is not totally devoid of a volitional component. There is a splendid editorial I like to cite by Dr William Bennett that appeared in the *New England Journal of Medicine* when leptin was first discovered, the circulating protein that reports to the brain on the size of the body fat mass (Bennett 1995). He said that individual instances of snacking, for example, appear to be totally random and under voluntary control. You raid the refrigerator one evening, you eat more heavily on week-ends, you skip lunch and so on, and yet, without continually consulting a calorie counter, at the end of 2 months, your weight is more or less the same as it was, which is really quite remarkable. Bennett says that, in the individual instance, these acts seem to be under voluntary control and almost random, yet, over the long haul they seem to have what he calls 'biological inevitability'. For me, this has two implications: first, that free choice is partly an illusion, and secondly, that choices about the timing and size of any meal or snack are embedded in a larger biological control system which operates over longer intervals. I believe similar statements can be made about alcoholism.

*A: Where then does volition enter?*

*EG:* It seems to me that in any individual there are diminishing roles for it as alcoholism develops. There are simple

and practical things which can be said. If you come from a high-risk family and you're 20 years old and you know your father was an alcoholic, you should be watching your drinking very carefully. You do not have to know the genes to know that. Now, once the alcoholism has been established, then it is much less under voluntary control. This person wakes up in the morning, shaking and vomiting. It is hard to say that he is acting freely when he drinks to relieve withdrawal, or even when he has been abstinent for several months and feels this terrible hunger that we talked about before. If the person is sober, what is his responsibility? It is to do something about staying sober. There volition still plays a role.

*A: And Bennett's big picture?*

*EG:* But the big picture is far more complex. No one starts drinking in order to become an alcoholic, to develop cirrhosis, to beat his wife or to crash the car. So there is a long-term change in the individual that is not under volitional control. The nature of this change is a major subject of our genetics and neuroscience research. Individual episodes of drinking are not devoid of some voluntary component, but the totality of the behavior over time is subject to profound pathological control mechanisms. This does not make the drinking and its harmful consequences any more palatable to those living with the drinker. These issues will become increasingly difficult because as neuroscience explains more and more of brain mechanisms of cognition, appetite and decision-making, the roles of volition, free will, and responsibility will be harder to define.

*A: What does that leave for free will?*

*EG:* So where is responsibility going to be left? Are we going to say the patient is not responsible for anything? I do not think we want to say that. It is tempting to say that we could keep volition out of the brain, but I do not think that we want to go back to the old mind-body dualism which science is so busy discarding. In my opinion, part of the public's uneasiness, even though it is inchoate, is because these issues have not been clarified. So we have got to work on that and whether we will succeed in doing so in the next 10 years, I do not know.

## **THE NEED TO BROADEN THE PUBLIC'S VISION**

*A: Looking back on your career, what do you see as your most important contributions to the field?*

*EG:* I suppose what I have been able to accomplish at the Institute here. To be, essentially, a lubricant for the work of the very talented scientists we support and to do my best to see that the Institute remains secure. That means having very competent institute staff (many able people

were already here when I came) as well as doing my best for the budget, which has not done too badly. I cannot take full responsibility for that. We have grown with the NIH. We have been treated well by NIH and the Congress because our science is excellent.

*A: Bridging science and treatment—what success there?*

*EG:* We have made some progress in bridging the gap between the treatment and the research worlds. The treatment world has been hurt by skepticism about treatment, which is their own fault in not having been advocates of good data collection for many, many years. Now in times of financial stress, they find that they wish they had data. I have often maintained that if data collection had been part of the treatment system, what was not working would have been discarded, and what was working could have been easily defended from the the skeptics in Congress and the insurance industry. That is changing now. There is a new interest in science partly catalyzed by these financial hardships. But the interest in science is due also to the fact that a new generation of younger, well-trained and sophisticated people are entering the treatment world. There have been welcome changes in the reverse direction. There are now many more researchers who are interested in dealing with the clinical world. The abyss between the treatment world and the research world, I am very happy to say, is closing. The Institute, with some role for me, can take some credit for that.

*A: Where do you still have problems?*

*EG:* Where we still have problems is with the public. The public is thirsting for scientific information, but they, themselves, are wrestling with their own ambivalences about alcoholism because it's so difficult to live with an alcoholic. That dilutes goodwill and willingness to listen. I remember one month—the residents spent a month

with us on the program—a resident came up to me at the beginning of his tour and said to me, 'Dr Gordis, I'm going to be frank with you. My brother is an alcoholic. He made life hell in our family. I don't like alcoholics. I am going to do my job as best as I can, but I think you ought to know what I feel from the start.' Well, I heard it, and during the month, as a result of teaching I have told you about before, he learned something about alcoholism and came to understand that his brother—obnoxious as he was when he was drinking—did not start out drinking to do the things he did to his family. I will not lie to you and say that I had turned this young man around completely. But at the end of the month he told me that his vision had been broadened and that is what we must do with the whole public.

**'A resident came up to me at the beginning of his tour and said to me, "Dr Gordis . . . My brother is an alcoholic. He made life hell in our family. I don't like alcoholics." . . . But at the end of the month he told me that his vision had been broadened and that is what we must do with the whole public.'**

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