JONATHAN O. COLE

Interviewed by Carl Salzman

Cambridge, Massachusetts, October 8, 2008

CS: Good morning. I am Carl Salzman at the home of Dr. Jonathan Cole in Cambridge, Massachusetts. It is Tuesday morning, October 8th 2008. We’re here to talk with Jonathan about his remembrance of the ACNP, and his role in matters related to the organization. Jonathan, perhaps we could start by you just telling a little bit about how you got involved in Psychopharmacology?

JC: Well, I’ll give you the shortest version. I was in Washington, working for the National Academy of the Sciences two years after my three year residency in Psychiatry at Payne Whitney and my two years in the Army. They advertised the job to everybody getting out of the service that year and I took it. One of the Committees of the National Academy was supposed to be advising the Army on research but the Army did not want to be advised. So, when the new drugs Thorazine (chlorpromazine) and reserpine came along they told me to go to the NIH to find out what scientists were doing there with the new drugs. They were not doing much. Ed Everts was doing studies on the effect of drugs on brain function and Steve Marchetti was studying biochemical abnormalities in schizophrenia but they didn’t have any clinical work going on. They were also starting to organize a big conference on how to evaluate psychiatric drugs and needed somebody to run the conference. Ralph Gerard, an eminent neurophysiologist, was going to be the ‘lead-man’. To make a long story short, I became the ‘wing-man’, the coordinator of the conference!

CS: Now, could you say something about the creation of the Psychopharmacology Service Center?

JC: What actually happened was that while we were working on developing the conference that was to take place in the fall of 1956, Mike Gorman and Nate Kline were testifying to Congress on the urgency of providing support for research with the new drugs. Some people were saying that the new drugs were totally ineffective and psychoanalysis was the key to any therapy in psychiatry, but Nate Kline and Mike Gorman testified and persuaded the congress to provide two million dollars to the National Institute of Mental Health to do a big co-operative study in state hospitals, run by medical schools, to find out whether they work or not. So while we were preparing for the conference in October, grants, in the amount of the two million dollars were allocated for Psychopharmacology research. It was a real first step. The NIH, needed somebody to run the program and I was available. I don’t think anybody else applied. It was handy that I was a psychiatrist and had had some experience with committees. So, I got the job.

CS: What year was that?

JC: It was the summer of 1956.

CS: And, then Gerry Klerman came along?

JC: That was later. I’d been lucky in setting-up the Psychopharmacology Service Center (PSC). Sherman Ross, a psychologist with many friends in many places helped me recruit excellent psychologists. A year or two later, somehow Massachusetts Mental Health Center sent Gerry Klerman down to work with me. He was followed by a series of young psychiatrists, A couple came down and spent two years with me and have gone on, mainly to better jobs.

CS: That’s how I first met you; I went to work for you at the NIMH in 1967. But by that time, the PSC was well established with many, many wonderful people. Along the way you had created the early clinical drug evaluation unit network.

JC: Yes.

CS: When and how did that start?

JC: My time points are unclear. We were involving nine hospitals in a comparative study of Thorazine (chlorpromazine), Mellaril (thioridazine), Prolixin (fluphenazine) and placebo in schizophrenia and in the course of that process, I would guess about 1959 or ’60, my staff, working with doctors who did early clinical drug studies, saw that these doctors were going from one little study to another little study without having any enduring support. So, I thought it would be a good idea to have some kind of grant program to support them, to carry them along in order to be able to do their research on their own and not drug company directed. I persuaded Dr. Shannon, the head of NIH to support it at the time. Then, Bob Felix succeeded Shannon and became the head of NIMH. For ten years he was testifying annually to Congress about our budget and people like me would help him fill-in the typescript of the actual testimony.

CS: This was in the 1960s?

JC: Yes. One of my chief deputies, Sy Fisher told me in recent years that he learned administration from me. My reaction was, huh, I didn’t know any administration. Actually, what I saw my main task was preparing letters to Congressmen and to the White House. I turned out to be good at responding to all kinds of irrelevant questions. So, I would answer all the requests and that would free up my staff to do the real work, to get the studies going.

CS: You were there at the inception of the phenothiazine era.

JC: I enjoyed watching drugs develop and seeing whether they would blossom or not. I think as time has gone by we had less good drugs and more elaborate and dubious studies.

CS: Do you think more dubious studies now then there were then?

JC: Yes, I think so. You know, my final will and testament, I guess, is that if you’re working with a drug in 100 patients and a few of the patients hadn’t said, ‘Wow, do I feel better’, then you probably haven’t missed anything and the drug probably isn’t going to turn out better than the placebo.

CS: Now, also in those early years, antidepressants began to come along

JC: Yes.

CS: You had imipramine and amitriptyline first and then things began to expand. How did you see that?

JC: The more drugs we had, the more we found that every new drug seemed to find a handful of patients that weren’t responding to the old ones.

CS: It was you and Gerry Klerman who created the first large-scale, multi-site study to study the effects of new drugs in schizophrenia. .

JC: Yes. He and I and Sol Goldberg did. Well, actually, the VA ran a study before we did, but we did the first one that was outside the VA. And I had learned from the VA study. Prior to their studies in schizophrenia, the VA had been running several multi-site studies in tuberculosis, but this was before I came along.

CS: I see. And then you got involved with lithium,

JC: Yes.

CS: Tell us about that.

JC: I had heard and read about lithium. I think by that time, Ralph Gerard’s Ypsilanti State Hospital research unit had Sam Gershon who worked with lithium as a resident in Australia. We went out there and got educated about it and the FDA kept lithium alive. A guy named Merlin Gibson, who was not a psychiatrist, was sympathetic and let lithium carbonate to be given as an investigational drug to almost anybody who wanted to give it to almost any patient. Then we got two double blind multi-center clinical studies going and the complexities of life began because in the two cooperative studies we didn’t get the same answers.

CS: What were the answers they gave?

JC: Well, in the first study lithium worked pretty well. In the second one we got mainly lithium failures. We figured that we had a different group of people in the second study. By the time of the second study lithium had gone on the market.

CS: So, what happened next?

JC: I got mildly irked because an upstate Minnesota group had been working with lithium and they could have been given the right to market the drug earlier but they were held back until Pfizer and Smith-Kline-Beecham were ready to go on the market and that was sort of unjust, I thought. But that was not my department.

CS: OK, and then the last group of new drugs that were being developed in those years were the benzodiazepines. What do you remember about those?

JC: Well, I think they had been subject to bad advertising as time passed. I’m currently bouncing in and out of a hospital, and when you get in there and get upset, they’re happy to give you Percocet a fairly powerful opiate but they won’t give you diazepam for sleep. Whether they’re right or not, I don’t know. So it’s become a nightmare.

CS: What about in the 1950s and ‘60s?

JC: Meprobamate came just before the benzodiazepines. It hit the market before the Psychopharmacology Evaluation Conference in 1956 and Wallace labs wanted to be included in the group participating in the conference.

CS: Was Wallace Laboratories the manufacturer of meprobamate?

JC: Yes.

CS: Then, Roche was releasing Librium.

JC: That came later.

CS: OK. Now, turning to the ACNP, do you remember how it got started? Who got the idea?

JC: I suspect it was Paul Hoch. Paul Hoch and Ted Rothman, a psychoanalyst in Los Angeles who used drugs in psychotherapy, held a meeting in the Barbizon in New York. Joseph Wortis, I, Fritz Freyhan, Heinz Lehmann, and I can’t remember who else, about 15 people were there.

CS: Could you name some of the others?

JC: Doug Goldman, I think. They have records in Nashville, as to who were there.

CS: Did someone think up the name ACNP right at the beginning or did it come along later?

JC: I presume it was Joel Elkes, but I don’t know when.

CS: If you think back to that early meeting, who would you think were most important in establishing the ACNP?

JC: I think Paul Hoch was one. Ted Rothman was sort of the driving force who would travel around and do almost anything to get it started. Paul Hoch was the senior commanding officer, the Dwight Eisenhower, of the operation.

CS: How did the meetings in Puerto Rico start?

JC: The group didn’t meet in Puerto Rico for several years because Hoch thought it was inappropriate. Well, there were other people like me who thought that meetings in Puerto Rico would be sort of fun. Then Hoch died and we moved to Puerto Rico. It did turn out to be good. We had meetings in the morning and then, like three hours around the pool and meetings in the afternoon. It worked fine, until we got too big.

CS: Well, we’ll get to the size in a minute

JC: Yes.

CS: Did the CINP also start around that time?

JC: It was sort of established by then.

CS: Now, the ACNP started as a small organization.

JC: Well, I think it was eighty some people.

CS: Who were the original people who attended? Were they mostly just researchers?

JC: It was a mixture of laboratory researchers like Peter Dews, and clinicians like Fritz Freyhan. We had working groups of people who seemed to enjoy the same topics, so they would discuss their recent findings.

.CS: Were all of the annual meetings in Puerto Rico in the beginning?

JC: One out of three or four were back in the States. Then we began to have meetings also in the west.

CS: Did the ACNP have any other function early on, or was it just an annual meeting?

JC: I think we reviewed a policy statement coming out of the FDA at one point or another and I know we gave a statement on tardive dyskinesia whenever that became prominent.

CS: That, tardive dyskinesia, was George Crane’s area.

JC: Yes.

CS: Were the ACNP and the ECDEU working together?

JC: They had an over-lapping membership. We would all attend meetings in Puerto Rico.

CS: Were most of the people who attended those early meetings academically based or were there some private researchers who were operating independently.

JC: It was a mixture.

CS:Did your own work and the ACNP interact at any point?

JC: We provided research funds to the ACNP at one point, early on. I managed to have them apply for and get a grant to support for four or five years, which was, I think helpful.

CS: Were drug companies invited into ACNP right from the start?

JC: Yes.

CS: Do you think that was helpful to the organization or did it interfere with free exchange of information?

JC: I think it was helpful. I think without financial support, a certain amount of spark from drug companies they wouldn’t have gone forward.

CS: Did the posters start out right at the beginning or was that a later innovation?

JC: Probably five to seven years after the ACNP was established.

CS: Did the drug companies would submit posters as well? They do now. Did they do it back then?

JC: Probably, I don’t remember there being any exclusion on them.

CS: I see. Do you feel that the posters from drug companies were helpful?

JC: We thought they were interesting. Nobody was really worried about investigators’ arms being twisted or their minds being bent by drug companies.

CS: All right. Well, in the early years, did you feel there was any conflict of interest?

JC: No, I don’t think so. I think that people followed their own ideas and decided what they wanted to. We realized the drug companies had a bias and they probably realized we had a bias and we did our own studies.

CS: Was the ACNP largely about getting money from the companies?

JC: The committee on drug dependence had developed a model of getting drug companies to put money in. And they had meetings with industry and investigators and the whole thing worked out. Nathan Eddy was the guy, a chemist at NIH who masterminded all that.

CS: So that was a model for ACNP?

JC: Yes.

CS: And for the ECDEU?

JC: Yes.

CS: So now here we are in two thousand and eight and there’s a great deal of concern about possible conflict of interest, do you have any thoughts about that?

JC: I think it’s really over-blown, exaggerated.

CS: Do you feel that the ACNP itself has been influenced too much by the presence of drug companies and their money?

JC: No, and I’m not sure which directions the drug companies wanted us to go in.

CS: OK. Do you have any particularly fond memories of the early years of ACNP?

JC: Oh, I wish we had recording of what happened at the annual meetings when Heinz Lehmann introduced me as president. He gave a very nice speech about me; I would love to have a copy of it.

CS:OK. Let’s jump and let me ask you if you were president of ACNP today, would you do anything differently?

JC: I’m not sure I would.

CS:Well, let me ask you a few specific questions.

JC: OK.

CS: Do you think the ACNP, the organization, or the annual meeting has gotten too large?

JC: Yes.

CS: Would you continue to hold annual meetings in nice resort-type places?

JC: Yes.

CS: Why would you do that?

JC: Well, everybody likes it and I think more people are talking to each other.

CS: So, you feel one of the great values of the ACNP is this informal discussion that goes on.

JC: Yes. I think so.

CS: And you would continue to have drug company presence?

JC: Yes.

CS: As much as it is today?

JC: I would probably continue as it is. I just don’t know of any negative or unethical or embarrassing event for the organization that they have done.

CS: In terms of the length of the meeting, would it continue to be more or less as it has been?

JC: I think five days from Sunday through Thursday is probably as long as anybody can stand.

CS: Now, what about activities of the ACNP now, as compared to the beginning? Do you feel that the ACNP should be more involved in political discussion or less; more involved with academic matters, FDA matters, etc?

JC: I think it should be more involved in advocacy matters with the FDA and, I guess more involved in political matters. I just don’t know how much that would cost.

CS: Do you remember how ACNP’s involvement in advocacy matters started?

JC: Danny Freedman was the leader on that issue by testifying on the hill.

CS: Do you remember what the testimony was about?

JC: I know that part of it was about an opiate related issue.

CS: I remember that Danny Freedman was very interested in LSD. Did the ACNP get involved in the LSD controversy at all?

JC: No.

CS: You set-up ECDEU which now is called NCDEU as a group of researchers who could individually or collaboratively do psychopharmacology research without the drug companies.

JC: Yes.

CS: So, they were conflict free. Do you see a role for some organization like that again?

JC: Oh, it’s still going and it has a meeting annually in the spring in Florida.

CS: That’s correct, but it’s not being funded by NIMH anymore.

JC: Only in the last two or three years

CS: Do you think that the ACNP should have any role in such an organization, either supervisory or financial or collaborative?

JC: It’s certainly worth thinking about it but I can’t tell whether it would be better or worse.

CS: I just wanted to say one more thing to those who will be watching listenig this tape: I went from the Mass Mental Health Center to work with Jonathan from 1967 to ’69 and my experience with Jonathan at that time was that he was a they superb researcher and clinician. Jonathan, as the leader, had in his head a wealth of information about psychopharmacology. So, in the pre-computer era, if we needed an answer to a psychopharmacology question, we simply asked Jonathan. And Jonathan would look up at the ceiling, and say, for example, ‘Well, let’s see, a study was done by some Hungarian psychiatrist with 1,200 people, 700 were male, 500 were female and the average age was so and so, the doses of the drugs given were so and so, and that was the outcome.’ And, that, frankly, I think he was a better resource than what we have now.

JC: Things get too big. My information system was based on key cards and several thousand references.

CS: Iremember that.

JC: It worked very well. They expanded it to the mental health information system with a small database and staff, and then the system fell apart. You just couldn’t get a reliable coding system of that size.

CS: Let’s see if we can just name some of those people at the PSC?

JC: OK. Sol Goldberg was an administrator and then he became a co-investigator. Sy Fisher got into side effects studies in the community at the University of Texas, Galveston branch. Martin Katz ran a big depression study at Einstein mainly with the people in Texas.

CS: And still is.

JC: And still is. Mitch Balter ran a bunch of studies on the use of illicit drugs, internationally.

CS: Mitch was a force of nature.

JC: Oh he was. He couldn’t write, but you could team him up with people who could write and run studies. He had all the ideas, they’d run the studies. He was great.

CS: There was Jerry Levine

JC: Jerry Levine was the psychiatrist who spent his time down there but there was a guy earlier than him who was my deputy.

CS: Irene?

JC: Irene Waskow did the psychotherapy study.

CS: And Al Raskin?

JC: Al did a depression study and moved to Detroit. And…

CS: George Crane.

JC: George Crane certainly documented the existence of tardive dyskinesia.

CS: Well, all of those people who were there in the early 1960s, played major roles in the ACNP as well. And we should also mention Gerry Klerman and Roger Meyer and Dick Shader and the other Mass Mental Health Center trainees who came through under your guidance. Thank you Jonathan very much.

JC: Thank you

CS: Great to talk with you.

JC: Thank you for coming. Thank you for doing it here.

CS: And, congratulations to the ACNP. It is the best meeting that I go to every year. It is the meeting I’ve learned from the most. It is the organization that I feel the strongest loyalty for and I love it.