CARL SALZMAN

Interviewed by Roger E. Meyer

Waikoloa, Hawaii, December 11, 1997

RM: It's December 11, 1997. I'm Dr. Roger Meyer and it's my great privilege to be interviewing Dr. Carl Salzman* in conjunction with the ACNP Task Force, recording the great figures in psychopharmacology. Dr. Salzman is professor of psychiatry at Harvard and the premier clinical psychopharmacologist in the Boston area. He's also been a major figure in developing the field of geriatric psychopharmacology. Carl, what got you started on this trail?

CS: That question goes quite a bit back. I was in medical school and I had no idea whether I wanted to be a psychiatrist. In fact, I was pretty sure I didn't want to be a psychiatrist until I started reading Aldous Huxley and became very involved in reading about mescaline, LSD and peyote. I met Timothy Leary and became very interested in psychiatry through that meeting. Those interests led me to the Massachusetts Mental Health Center, a year after you went there.. And there, I met numerous stimulating faculty, and residents, who were to have a fateful effect on my life. Perhaps the most influentials were Gerry Klerman, and Dick Shader along with Al DiMascio. One of my early supervisors was Eric Kandel; another supervisor was Ed Sacher. In addition to becoming enthusiastic about psychodynamic concepts and psychotherapy, which I still am, I also became enthused about psychopharmacology. I began to do research on benzodiazepines as a resident with Dick and with Al DiMascio. Al took me to a CINP meeting in Washington in 1965 or '66. He introduced me to Jonathan Cole and said, "Jonathan, Carl should work with you". And, Jonathan, of course, immediately offered me a job running the Early Clinical Drug Evaluation Unit. So, I spent my NIMH years working with Jonathan Cole in the Barlow building in Chevy Chase, Maryland from 1967 to '69. By that time, I had already published several papers alone and with Dick Shader. The experience at NIMH and the ECDEU program allowed me to expand my vista in psychopharmacology. I had an opportunity to meet many non-Boston researchers and clinicians -a revelation that there were knowledgeable psychiatrists outside of Boston

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who had different perspectives than the ones I had learned as a resident - and, at the same time, became tremendously excited by the growing number of available psychiatric drugs, mostly neuroleptics. Lithium had just made available; we were using imipramine, amitriptyline and Sinequan (doxepin), as the primary antidepressants, with a little bit of MAO inhibitors, and Librium (chlordiazepoxide). Dick Shader was back at Mass Mental Health Center, having finished his NIMH training, and he, very much, insisted that I return and work with him after my two years at NIMH. Although, my wife and I had considered trying San Francisco, I couldn't resist an offer to return to Mass Mental Health Center. So back we went to Boston, which was home. I've been at the Mass Mental Health Center ever since. For the first ten years on the faculty, I worked as a colleague of Dick's, teaching psychopharmacology, helping him create a first-class psychopharmacology teaching program in a psychoanalytically oriented training program and collaborating on benzodiazepine research. At first, we conducted clinical trials, but Dick became interested in benzodiazepine pharmacokinetics and I became interested in geriatric psychopharmacology. At that time there was almost no psychopharmacology research or controlled clinical trials in geriatric patients or research in normal volunteer subjects.

RM: What provoked that interest?

CS: I don't actually remember, except that we had, in the course of one or two of our pharmacokinetic studies, a few older people and we realized that they responded differently. Dick and David Greenblatt were just getting interested in pharmacokinetics, and, the kinetics of some benzodiazepines, were different in the elderly from the adults. So, suddenly, I realized that geriatric psychopharmacology was like psychopharmacology had been ten years earlier. It was a new frontier. There was no information. It was incredibly exciting to be in the forefront of the field. So, we began to look at psychotropic drugs in the elderly and one of the things that became apparent is how much fun it was to work with older people, for if you had a good relationship with your older subjects they started to tell you about their lives. If you have any interest in history at all, you get history from people who lived at the turn of the century. And, in Massachusetts and New England, you get a fantastic survey of how the world has changed since the

beginning of the 20th century. So a bonus, in addition to doing the research, I was getting to hear some amazing personal histories.

RM: You had to do a number of pieces in methods development.

CS: We did a lot of methods development and rating scale methods development, which was still in its infancy in geriatrics. We were doing the kinetic work, which clearly showed changes in oxidative metabolism in the elderly and prolonged half-life of drugs. And, dosing had to be individualized, and, generally lower. The pharmaceutical industry did not have any guidelines for giving drugs to the elderly. Basically, they said, use lower doses, which they still do, but we didn't have any precision about actual necessary dose adjustments. Diagnosis of the elderly has fascinated me. In depression, e.g., the characteristics in over 80 year olds is quite different than in those between ages 65 and 80. Depression in the between 65 and 80 years old more resembles the depression in young middle aged adults than in the very elderly. In the over 80 year olds the chief characteristics of depression are irritability and withdrawal of social and interpersonal interest, as opposed to sadness, helplessness or vegetative signs. This may be even more relevant to the very elderly, over 100, who are now the fastest growing age group.

RM: Are there measures that people are using?

CS: Well, we're creating them right now. In fact, we're completing a double blind study of paroxetine, in over 80 year olds in a nursing home and one of the findings has more to do with the diagnostic discrimination of depression than with the patients' response. But, it's hard to make a clear-cut diagnosis of depression. When you ask some of the patients who are over 80 standard Hamilton Depression Scale questions, you realize that they all have sleep disturbance and they all feel relatively hopeless about long-term survival. If you ask an 85 year old how they think about the future, they will all say, what future; I might be dead tomorrow. But, when you ask them about social interests, and they say, well, I just don't feel like going and being with other people; I'd rather stay in my room that is one of the early signs of depression. And, irritability becomes worse with old age.

RM: When you look back as your work has evolved which individual or individuals do you think have made the greatest impact on your thinking in a sustained way? Part of it, obviously, is without mentorship, but there may have been some early mentors.

CS: Well, there are people that I always learn from and when I come to these ACNP meetings. I try to, either, talk with them or go to their presentations. I always feel like it's something new. You are one of them. Dick Shader was one of them, and, of course, Gerry Klerman was one of them. Jonathan Cole was also, but Jonathan doesn't come to to many meetings any longer.

RM: Jonathan Cole?

CS: Jonathan Cole. I almost always learn something useful from Ross Baldessarini. I almost always learn something useful from Charlie Nemeroff and Alan Schatzberg, who was a student of mine. You notice I'm identifying, primarily, clinical researchers, because I think it's important to clarify that I am a clinical researcher and teacher, rather than a basic science researcher, so the people that I tend to associate with do their work in the clinical area.

RM: It's really striking about your work the way you think about these issues. It's characterized by methodological rigor and an extraordinary degree of humanistic concern about people, and, you communicate both in your teaching.

CS: Well, I appreciate the comment.

RM: Well, it's true.

CS: I think that the one thing that always troubles me about the ACNP meeting when listening to the clinical research presentations is that there is not enough attention paid to real life human beings. It is almost as though the human beings are described as a collection of receptors or second messengers or gene expressions and other "neuroscience stuff" rather than suffering human beings. And, that makes sense if you're doing research. But taking the research results from these meetings back to the real-life clinical world, and, applying them to patients, requires a shift in understanding and application of the complexity of people's lives, because the diagnoses and treatment results are not as clear as it might appear when presented at these meetings. Depression is not just hypercortisolemia or what shows up on Hamilton's rating scales. That's not what depression is. And, yet, we sometimes think in simplistic ways because we're trying to understand basic disease mechanisms which may require temporarily reductionistic thinking. But I sometimes worry that, in our psychopharmacology research field, we are

creating a generation of younger investigators who don't quite understand the clinical application or the complex realities of clinical treatment with these drugs.

RM: One of the things that you've really done in an extraordinary way in your educational programs, which you pioneered at the Mass Mental, has been to figure out ways to communicate the complexity by using case methods and other approaches.

CS: Well, I received a New York State research award given to me by Heinz Lehmann last week and Heinz is somebody who I would very much identify as a person worth emulating. What Heinz taught me, back when I was at NIMH, was the importance of being a good clinician He taught me looking at the individual, as well as the whole body of data that might apply to the indiviual; looking at the patients and not just the mean changes on rating scale scores in the treatment research. One thing that Heinz could always tell, in a sensitive way, whether the patient was responding or not responding to the medication without rating scales and all kinds of fancy high tech stuff. And, of course, you were trained in that tradition, as I was, and Dick Shader, and Gerry Klerman and all the other Mass Mental Center residency graduates who went into research. The point that I'm leading up to is that to be a really good researcher, you have to be a really good clinician. And, to be a really good teacher, you have to be a really good clinician and a really good researcher. The way to combine all three of those is using the case presentation method, in which you can take a patient and illustrate the larger research findings through implications and, then, also illustrate how the patient may not correspond to the specific findings of any research application, because patients, like all of us, are different. We're different from one another and we may respond in a "mean" way, but we also have "standard deviations", so to speak; we are individuals. And, that individuality brings teaching alive. That brings psychopharmacology alive and that's what we do at Mass Mental Health Center, and, if anything, I'd like to do more. If there was one area I would hope the ACNP might want to explore in its teaching role, as it did with the model curriculum, is creating a series of model teaching cases, based on real people, to illustrate some of the most exciting research areas that we're involved in right now, say, the new antipsychotics or the new mood stabilizers, the gene transcription potential theories, and, illustrate them through a patient.

RM: Do you see the potential through your own involvement over the next decade as trying to help to move the field in this direction?

CS: I see this next part of my career as almost exclusively doing that. I think that I will always be a clinician and always be a teacher and I'll always be a dabbler in psychopharmacology research, compared with most of my colleagues here. But what I really want to do is to try to bring what I learn here at the annual meeting back to the students that I teach and the community of clinicians and, to that end, I have, for the past almost 15 years, summarized the meetings. I sit down with my computer in my hotel room during the meeting and I type out the salient features of the abstracts or the presentations. I've gone to organize them by topic, and try to make them readable and understandable. If I can understand them, then, I think others can also understand them. And, then, I go home and distribute this note to the residents and the faculty. I hope to do more of that and, maybe, even expand it into the case base teaching method, as well.

RM: So many of your junior colleagues, who have been through the Mass Mental, identify you as the singular most important teacher and mentor that they had at the Mass Mental. One of the problems that we, as a field, face, but also all of medicine faces, is how to get people to recognize the importance of that mentorship role, and how do you generalize, from Carl Salzman to the larger community, to try to infect people with that enthusiasm, infect people with the importance of that piece of psychopharmacology.

CS: Well, you know, you've just given the answer to the question. You have to be enthusiastic yourself. You have to be a little bit lucky. I think I was lucky. I, you know, got to know people like you and the others at the Mass Mental Health Center, and was infected by their enthusiasm. Can you imagine Eric Kandel being a psychotherapy supervisor?

RM: It was incredible.

CS: With Gerry Klerman in the morning, we residents would talk about urinary catecholamines and then, in the evening, we'd go to his house, eat pizza and read Freud, with the same man. I mean, I wanted to be like him. I wanted to be like Dick Shader. I wanted to know all of this neurobiologic and psychoanalytic information and synthesize them together. I think you have to have the kind of enthusiasm that Gerry communicated daily. You have to really feel it and I think some people do and others have a passion in

other areas, which they communicate. I think, without the passion, without the belief in it, it doesn't come across. Then, you have to find the willing student, somebody who's kind of interested but not sure and turn them on. If you can do one a year, it's a great gift.

RM: That's what happened to you in medical school. I mean, you really weren't interested in psychiatry at all.

CS: That's right.

RM: But, you got captured.

CS: I got, literally, turned on, as well as metaphorically. You know, there are many, many people at this meeting who trained with me, but the one who stands out as an example is Danny Weinberger, who was our chief resident in psychopharmacology. During his third year of residency, Danny had many talks with me and with others about what was he going to do with his career. I remember him standing at the door to my office; he was going to go to NIMH and I, basically, said, you know, Danny, find something that really excites you and just ride it as far as you can and your passion for it will keep you going and that's what you really want to do. And, he, very quickly, found schizophrenia and, my pleasure in having had a little bit to do with Danny's education and his career is endless. I just came from his session and it's just wonderful to see his passion continue to grow and provide us with exciting new discoveries.

RM: To APA meetings and here you would often bring young colleagues. You always push forward them to meet so and so and, then, so and so.

CS: Well, that, I learned from Al DiMascio. He brought me to my first scientific meeting, a CINP congress, and he made sure that I shook hands with everybody, knew which meetings to go to, have some fun and learn something. So, whenever I have funds and an interested student, I will bring them to the ACNP. I think Oakley got annoyed with me one year. I brought 5 or 6 people to San Juan and, so, the rules about how many guests you could bring got tightened a little bit. But, I think that's the way to do it, and, of course, the ACNP is such a fantastic organization. If you bring someone who has any interest in psychopharmacology to one of these meetings, they're hooked. I mean, they say, "this is the best meeting I've ever attended", which it is. It is for me and that's why I do it for them.

RM: Let me refer you a bit back into the past. When you and Walter Pahnke became involved in hallucinogenic research, you had a very strong interest in looking at subjective states and so forth. Do you think that the whole issue of hallucinogenic research has petered out or do you think there is still some potential in it that people should be exploring?

CS: Wow, that's a great question! The answer to the latter question is definitely, yes. It, first, was a political problem. The drugs, of course, were misused and that became politically unacceptable. They also became scientifically unacceptable.

RM: Did you find that in your own early career?

CS: No, not at all, not at all. I still think that careful research into subjective experience, using these drugs would have a lot to offer to psychiatry, psychopharmacology, and students of brain function.

RM: What would it offer?

CS: Well, the kind of alteration of reality and subjective experience that these drugs can produce is unlike any that I or many others have ever experienced. It's not like being drunk or stoned or meditating or hypnotized and it's not like dreaming. Of course, we know these drugs affect serotonin function and they do produce some psychosis-like features. Although what they produce is really not a model psychosis, they produce a heightened awareness of one's own mental processes. The problem is, that it's very hard to study the experience and very hard to model it, because it is completely subjective. The term we used to use was "ineffable". That was one of the reasons I got very involved in the measurement of subjective experience and of placebo response. Some of the early work I did at the Mass Mental Health Center, and I still have some interest in it in my present work, is the understanding the subjective experience of different mood states, because except for vegetative and autonomic signs, they are subjective. How do you know when somebody is anxious? How do you know when you are anxious? I ask my patients, "how do you know you're anxious; how do you know you're depressed"? Then, if the descriptive words are more or less agreed upon, we more or less, understand each other, but it's always an inference.

Another problem with these drugs arose, and I really think neuroscience and academic researchers were a little bit to blame for this. It is characterized by a discussion

I once had with Danny Freedman, another one of our great mentors and somebody who could synthesize all science and who also loved to philosophize, either at the ACNP or on long airplane trips. We were on an airplane from LA to Boston together, and while getting acquainted, we got into a discussion about hallucinogenic drugs; he was very much against researchers taking LSD. He said, "you don't have to be psychotic to study schizophrenia and you don't have to make yourself psychotic to study these drugs". While I can't disagree with that opinion, I've had that argument with him in my mind over the subsequent twenty years, even though he's no longer here to argue with. He's not right! It's true, you don't have to be schizophrenic to study schizophrenia, but if you are or have been or know somebody who is and you've seen the disease in all of its' forms over twenty-four hours, week after week, you understand something about it that a psychiatrist or researcher who sees the individual in a brief cross sectional time frame, never gets. And, the same is true of subjective experience. The more you can personally understand what your research subjects or your patients are experiencing, I think the richer your research experience will be, the more informed your research questions will be and, ultimately, the better informed your teaching and clinical practice will be. Now, I'm not saying that everybody ought to take LSD, because those days are over, fortunately. But when we think about LSD, or any of the psychotomimetic as drugs whose only function is to kill serotonin cells, it's as though we have literally thrown the baby out with the bathwater. To illustrate this: two years ago I was talking with a patient, who had come to see me, who had severe OCD. He was a wonderful bright 28 year old kid, who was crippled by his OCD. He really could do almost nothing and he'd been to many doctors because of his dysmorphophobic symptoms, rituals and other things. The one thing that made him feel normal was MDMA, "ecstasy". He would get "ecstasy" on the street. He would take it and he would say, "for that hour, hour and a half or two, it wasn't just that I was high or euphoric, but I felt normal, the obsessions, the compulsions, the worries that I have all vanished. And, then, they would come back". Now, that's an observation worth following up, but, of course, it's hard to follow it up when you know that studying drugs of this class is going to kill serotonin cells and no ethics committee going to let you do it. And how are you going to find subjects if you're not going to take it yourself. And, if you generalize this conundrum to the whole

scientific field, it becomes very difficult to study the alteration of subjective experience with any chemical that doesn't have clear therapeutic value. After all, we don't advocate people becoming alcoholics in order to study alcoholism.

RM: Yes, but what you're suggesting is that we are missing an entire area of drug discovery, and, if we had an ecstasy that didn't kill serotonin cells, that would be a very important redirection for drug discovery.

CS: Yes, and I'm saying not only that, but I think we have all become frightened, both, by the political, as well as the potential neurotoxic consequences of these drugs and, so, we have abandoned an area of psychopharmacology research, which I think is potentially, clinically, amazingly rich. And that's sad.

RM: In a sense, Timothy Leary has met Aristotle. But, you're telling us to rediscover William James?

CS: Actually, well, that's absolutely true; to rediscover the original Timothy Leary before he became a showman. When I knew him in '61 at Harvard, he was not the way most people now think of him. He was a careful, sober, scientific thinker, who was really interested in the alteration of subjective experience and the psychological therapeutic properties of these drugs. It was only later that it all went in a different direction. Sad!

RM: There's another piece that people who don't have your solidity, got, caught up in. And, that was that you did with Richard Katz and Walter Pahnke in which you discovered the capacity of hallucinogenic drugs to produce shared subjective experience. That was really profound.

CS: Oh, that's another whole interview.

RM: I'm sorry.

CS: It's a terrific subject so..But you're absolutely right and, of course, it was poisoned science. It was anti-science; it was anti-intellectual. Ultimately, that's why I didn't continue in this area of research and, basically, severed all my ties with Leary although I did call him before he died.

RM: You did?

CS: I did. I hadn't spoken to him in twenty-five years but we chatted on the phone and I said goodbye to him. I reminded him of how important role he had played in my life. He

wasn't too interested in my being a psychiatrist, but he was very cordial and very friendly. He was dying.

RM: That's remarkable.

CS: Yes.

RM: Do you feel any disappointment that that part of your work was not really continued?

CS: No, I don't, Roger. I've had a very rich life. I've had a terrific professional career. I think I'm really enjoying now the benefits of the years of hard work and I feel very good about it. My regrets are not in that area at all. My regrets are, perhaps, more in the area of not having been a good enough, scientist and devoted more of my time to research, but I had so much interest in the clinical and the teaching area that I couldn't do it all.

RM: Yes, but you also decided early on where your passion was. Then, you followed your passion just as you told others to follow their passion and you didn't force people to be a Carl Salzman. You really forced a Danny Weinberger to be a Danny Weinberger. That is a remarkably quality for a mentor.

CS: Well, thank you. I never felt in competition with my students. In fact, the better they did, the happier I was. Just as a personal note, all of my familywere teachers. My father was a teacher and I remember him saying to me, once, you can do anything you want, but "don't be a teacher"! So, here I am, a teacher.

RM: What do you think about the Mass Mental? It was a great spawning ground of so many really outstanding scholars and scientists and, yet, the environment that you were trained in, it was very psychoanalytically based.

CS: Well, it was psychoanalytically based, but, again, it was a place of superior people, rather than just superior theories or monotheistic theories. If you think of the many people who were there and their enormous range of interests, it was like being in a university for me. It was possible to become involved in psychoanalytic psychology. It was possible to become involved in interpersonal and behavioral programs. It was possible to be a basic scientist researcher with the animal models of sleep, of affective disorders and, even, of schizophrenia. It was possible to be a pharmacologist and a psychopharmacologist.

RM: But, in your class of, say, 24 residents, there were you and Herb Meltzer. Who else went into psychopharmacology?

CS: Bob DuPont, myself, Ed Khantzia, and Herb, of course, is the preeminent alumni of our training group. I think that's all for psychopharmacology.

RM: So that it took a certain passion, as you had, to follow the psychopharmacology.

CS: That's true, but, if you recall, there was always a minority of people at that time who were interested in research and particularly interested in biologic research, and they almost always went to NIH. Remember, the shuttle bus between Mass Mental and NIH, and the Tuesday lunches where we would talk about the "old days at Mass Mental" and the new days in psychiatry yet to come. That was a very select group of people and I felt privileged and honored to be among them. The Mass Mental alumni, who populated NIMH on the campus as well as off the campus at St. Elizabeths Hospital, were fantastic people, and to be among them, I think, was the high point of my life. To be at Mass Mental and among those people, I think was clearly something that I had never ghought of that it would happen and, now, looking back, it is unquestionably the high point of my professional life.

RM: And, as you look over the history of the Mass Mental post 1960, you are the singular institutional memory.

CS: I am, I'm the one carrying the institutional memory.

RM: You're the one who can really identify it through to the point where it is now and that's an incredibly singular and significant role in American psychiatry.

CS: Well, I loved it. It now feels a little lonely, but you know, it was a special place with special memories.

RM: It's a very special role.

CS: Of course, people like you and I also have a memory of the ACNP, because it goes back thirty years, now, in watching the organization evolve and change and how it's worked out and that feels good, too. I must say, I feel very fond of this organization. The annual meeting is, unquestionably, the best meeting of the year.

RM: Yes. Is there some major question that I didn't ask you that you really would have loved to have an answer to?

CS: I thought you were going to ask me what I thought about the organization and how it's developed and what's good and what's not so good, some of the things we've talked about at our "annual beach" talk. I've given a lot of thought to those things and I don't know the answer. I'm also afraid that my comments are going to be misunderstood, so I have to be careful in how I phrase them. I have very mixed feelings about the relationship between our organization and the pharmaceutical industry. On the one hand, industry certainly supports many scientific activities. And, I also think that the meeting between the academic research community and the pharmaceutical research community is a tremendous area of cross pollination and fertilization that has led to great discoveries; I think it would be nihilistic and cynical to say otherwise. But, I think there's another side to it. I think we are all, including me, too influenced by industry in sometimes very subtle ways. It's rarely vulgar: nobody from industry ever says, "say this and don't say that" about our product. That would never happen, but the influence is much more subtle in terms of how we understand the clinical application of drugs, how we compare drugs and how we gather the data and present the data. You can see it here at the meeting. If you look at some of the posters in which studies of drug comparisons or drugs vs. placebo are presented, you know that the study is, in part, been funded by industry. You know it because you already are familiar with the work, so you have some basis of judgment. And you can see that there are statements that are not made, and information that is not presented, so there are data errors by omission. It's not necessarily lying, but there's subtle inference given that this particular drug is, say, better than that particular other drug for these particular patients, and here are the data., When you have had some experience with the drugs, or carefully examine the methodology, you say to yourself, "that's really not true". So it requires in all of us, a need to maintain a high level of scientific and clinical rigor in evaluating drug company data, because what we learn here at the meetings may, in fact, not always be, in fact, applicable or correct in the clinical world.

RM: You know, you just did a remarkable thing. I was thinking about it. You've benefited from industry support, your education programs, your research that you've done. You recognize the value of, what's been called the triangle, the powerful triangular relationship of academia, industry and government. It's like the way that you've

described the LSD and hallucinogenic drug potential for good and the ways in which it got carried away by due process. Your argument, basically, is to recognize the good, but don't become carried away by forces that subvert your own judgment. In that thinking, in the way that you described the dangers, as well as the benefits of the relationship, you also reaffirmed the Carl Salzman approach to the work, which is retain your individual groundedness; don't get carried away by movements and really stay the course in the set of very good principles.

CS: OK, you said that in such a nice way. Remember, in my work at NIMH with Jonathan Cole, I was running the ECDEU program, and as Jonathan originally created it there were no drug company people who participated in the investigators meetings. It was a small group of very gifted and sensitive investigators, who met several times a year to discuss their work without fear of interference or the consequences of what they were going to say, from industry. I don't think that's possible to do any more. The world was different then with fewer drugs and a smaller number of investigators; it was very special time. And, the discussions around those tables changed when there were drug company people in the room. I saw it with my own eyes. I wouldn't say scientific rigor hanged, but the level of openness changed; hard questions would not get asked when industry reps were in the room, because you might be stepping on somebody's company toes or because there might be financial or professional repercussions later on. Again, I want to emphasize that I don't think only "the good old days" are the only good days, but there has been something a little bit lost. I was wondering, in preparation for this interview, what would I want to do? I made a comment to the FDA Advisory Committee last Thursday, which I think would apply here, as well. We were discussing a post marketing survey of side effects at this advisory committee meeting, and the question of how do you get good, reliable and valid information about side effects, once a drug is out? Mainly, if it's not lethal and doesn't make the media, you get it from what the industry collects, as well as from spontaneous reporting to FDA. And, it occurred to me that we should resurrect the old ECDEU model. We should have, say, 10 or 12 designated gifted clinicians, Heinz Lehmann type people, from around the country, who observed the drugs in their clinical use, monitored the emerging side effects and, then, came together to discuss and compare and share observations. Did you see sexual dysfunction with

SSRI's? Did you see weight gain with the new generation of antipsychotics? Those kind of discussions; would provide a very effective early warning system. Taking that model and bringing it into ACNP would mean to have a small group of designated clinical researchers or, even, basic scientist researchers, meet, informally, maybe three times a year, maybe in conjunction with this meeting, to discuss amongst themselves, what they've observed, and the clinical implications of their research. The information shouldn't become public, but the scientific community could then be informed abut it without the influence of the industry. It might not be expensive and it might be practical.

RM: Do you know if the practice network that the APA is sponsoring is doing any of this?

CS: I don't know , Roger, but the other side of it is that the information, now, that we developed gets out on the internet in incorrect ways and, so, if anything, we're in a much worse position, in terms of misinformation or mischievous information, being disseminated than before. And, it would be nice to have a group of people meeting, who were not under any influence and could just look very hard at the data and their implications. After all, it's the implications of what we do that's important. I mean, we need to learn things for their own sake, but we're basically an organization of doctors, who want to help people.

RM: So, one of the functions that the ACNP could have in the future would be to try to foster this kind of unrestricted, uninfluenced research discussion.

CS: Right, and I'm concerned that the new society, the American Society of Clinical Psychopharmacology, grew up because the ACNP wasn't doing enough of this clinical work and I think that's regrettable. We need to keep the rigor in our work and that's what I think the ACNP does, to its' credit, but it has somehow abandoned a little bit of rigor on its' more clinical side, and that's reflected in these annual meetings

RM: What's been the impact of managed care in clinical psychopharmacology, as you've seen it?

CS: Well, there was a poster last night on the Treatment of Depression in Managed Care in Ten Thousand Patients, in which Sertraline vs. Treatment As Usual was studied, and compared with a special algorithm. People treated As Usual fared better.. But what is distressing is that the special algorithm was administered by non-psychiatrists. So, what

is happening, of course, is that many of our drugs are now being routinely prescribed by non-psychiatrists, which I suppose is not bad from a public health point of view if the drugs are used correctly. But, it certainly is marginalizing clinical psychiatry to take care of only the treatment resistant and the more complicated patient and the co-morbid conditions. I don't know whether that's good or bad, but basically I think it's bad.

RM: Where did that study come from?

CS: There were four managed care networks that collaborated. One was funded by Pfizer, because the government wouldn't fund it. I think, what's happening, is that psychopharmacology practice is being influenced by managed care pharmacoeconomics. Clinical observations, which then follow the pharmacoeconomics may not be accurate, but look accurate, because you have these large "N's" and you've phrased your questions in such a way that it looks like this algorithm, in fact, works. Well, that was a very easy study to criticize; it was a terrible study and none of us would have accepted it for a journal; they didn't ask the right questions and they didn't really have the right controls and they didn't really provide the right answers. But, they got Hamilton ratings. And depression is more than Hamilton ratings. But, that's one of the major influences of managed care and these large scale survey studies. Another major influence, of course, is that it's almost impossible to do inpatient research in community hospitals. And, of course, it's also almost impossible to find outpatient volunteers, because the managed care company would not let them participate unless they kind of sign wavers and say they're not going to get care through the managed care system. It's very worrisome. It's worrisome in teaching, too. All medical schools are finding very hard to teach psychiatry and the treatment of the seriously ill patient in managed care settings, because they are managing people, not really treating people. It's very different from the psychiatry that we learned at Mass Mental Health Center.

RM: We've certainly reviewed the history of ACNP, Mass Mental and Psychiatry and it is clear that you will continue to influence the next decade and more trainees.

CS: Well, thank you, Roger.

RM: Thank you.