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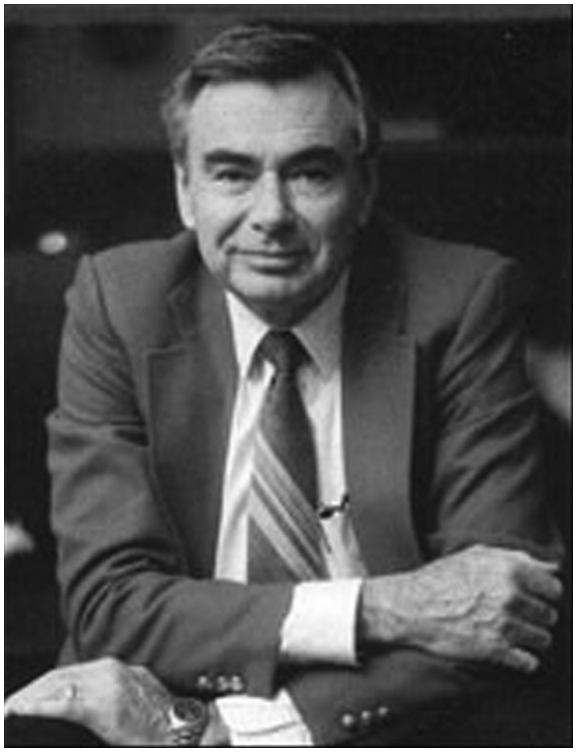
Conversation with Charles P. O'Brien



In this occasional series we record the views and personal experience of people who have especially contributed to the evolution of ideas in the journal's field of interest. Charles O'Brien is Professor of Psychiatry at the University of Pennsylvania. He founded the Center for Studies of Addiction at Penn in 1971 and led the team that discovered the benefits of opioid receptor blockade in the treatment of alcoholism, created the Addiction Severity Index and conducted numerous clinical trials on the treatment of addiction to opioids, alcohol and stimulants.

CURIOUS ABOUT SCIENCE

Addiction (A): How did you become curious about science and the laws of nature?
Charles O'Brien (CO): Well, actually, it began in high school. I started reading a lot about the chemical and physical world. My father was an entomologist and I helped him in his work. He had a private business, besides being in charge of federal government programs in Louisiana, so I learned a lot about insects and other animals at an early age. When I was in high school I did some experiments with what we called in New Orleans 'doodle bugs'. They are actually crustaceans. When I got to college I caught crayfish, which we called crawfish in Louisiana. I did genetic studies on them, raising them in the laboratory and studying the inheritance of striped and spotted chromataphore patterns and a little bit of Mendelian genetics.

A: Was this before you went to medical school?
CO: Yes, all this was before medical school.

A: Was there anyone else in your family who liked science, or were you the first person to go in that direction?
CO: Well, my father received his Bachelor's degree in entomology and I thought that the pursuit of knowledge was always kind of like the highest calling—even though I wanted to be in medicine at an early age. I was really attracted to developing new knowledge. I was always fascinated by evolution and I am still amazed that the majority of United States citizens do not believe in evolution. Even today, it is amazing. We lead the developed world in creationists.

'I was always fascinated by evolution and I am still amazed that the majority of United States citizens do not believe in evolution'.

A: At the time you were a child, was evolution an accepted thing?
CO: Well, it probably was not generally accepted, but it was in my family. They accepted the fact that this was reasonable and that there was nothing antireligious about it.

MEDICAL TRANSITION

A: How did you think of entering medicine? It is a bit of a step from entomology, bugs and crayfish to helping others.
CO: Actually, I was very idealistic and I thought about becoming a Dr Schweitzer—going to Africa—because I did not immediately think about becoming a researcher myself. In my first year of medical school I really took off with physiology and studying mechanics of the lung. I derived some new equations to answer questions on lung physiology. I enjoyed playing with models of cell membranes with a Langmuir trough. I was really fascinated by neurophysiology.

A: That led you to do a dual degree, MD/PhD. Did you earn them at the same time or sequentially?

CO: At the same time. I have always been in a hurry and actually I did 4 years of college in 2 years and got into medical school after 2 years. Then I began working on the PhD, I guess during the spring of my first year in medical school. I started taking courses with the graduate students as well as with the medical students and I took summer school courses all along.

A: So you were really on an accelerated track from the very beginning.
CO: Yes, I was. I do not know how I was able to juggle so many things. When I was a teenager I decided, after reading about Tom Edison, that I could teach myself how to get by on less sleep, so I did that, but then more recently I came across research showing that people who deprived themselves of sleep over time shortened their lives. So I have been trying to unlearn my short sleep habits.

A: When you were in medical school, did these interests in neurophysiology then evolve into an interest in psychiatry?
CO: Well, psychiatry was the highest form of neurophysiology and I was always interested in memory. I was reading every article that I could—actually I had a very obsessive way of reading the literature. I would go to the library. All the new journals would be put on a table before they were bound and I would read the table of contents of any journal that had to do with the brain or with the nervous system, to see if there were any articles I wanted to read. I would try to read every one that came in. In those days there were probably about 50 neuro journals. We are talking about 1960–65.

A: Was that possible?
CO: It was actually doable then. Now there are thousands of journals about the brain—it has really grown so much, but I was actually trying to learn everything that I could learn when I was young. Everything from the peripheral nervous system to the hypothalamus. It was embarrassing to be going into psychiatry because there was no knowledge base there; that is why, for my own self-respect, I had to get training in neurology. I took a Neurology Residency before psychiatry and became board-certified.

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A: It is extraordinary, the trajectory over the subsequent 4–5 decades. When you started in psychiatry, where did you do that training?
CO: I did college and medical school at Tulane University in New Orleans. I started taking courses in psychiatry in the second year and I did a review of antidepressants when I was a second-year medical student in 1961. I had a good teacher who turned out to be a member of ACNP, Donald Gallant. He was really impressed with my knowledge of antidepressants at that time. He could see that I was seriously interested and went well beyond what was in the textbook. I reviewed the literature and such. So that was kind of encouraging, and I even submitted a review paper to the *New England Journal* which was not accepted. I was learning how to submit papers and accept rejection at an early age. I did my first year residency at Massachusetts General Hospital, Harvard Medical School, and it was really pretty good for me to get out of the South and go to Boston, which was highly competitive. They had only 12 medicine intern slots and they had hundreds of applications from all over. They only accepted three of us who were not from Harvard Medical School, so I felt privileged.

A: Extraordinary!
CO: That was pretty interesting. I always was trying to get at the neurological basis of behavior.

A: And after the Harvard/Massachussetts General time?
CO: Then I went back to Tulane doing neurology and psychiatry simultaneously.

A: Dual residencies?
CO: I had a ward in psychiatry and a ward in neurology at the same time, and each department did not know about the other. I really enjoyed taking care of patients. I had a large number of patients and I could juggle my time.

A: This theme of making brain and behavior connections and also marrying that knowledge with clinical care had its roots really early for you in terms of basic research, clinical research and the combination.
CO: I was invited to spend my 2 military years at NIMH (National Institute of Mental Health), but the Navy would not let me go. I had to spend 2 years at the Philadelphia Naval Hospital. While still a medical student, I was awarded an MD/PhD fellowship in 1963, the first year that these were offered by the Life Insurance Medical Research Fund. They only gave out five in the country and I was lucky to get one. I started my two residencies in neurology and psychiatry at Tulane, did a year of neurology in London at Queen Square and then finished in Philadelphia at the Hospital of the University of Pennsylvania. I was invited to join a laboratory at NIMH for my

required military duty, but I was already committed to the Navy. I became a staff neuropsychiatrist at the Philadelphia Naval Hospital, but continued my research at Penn. I was already accustomed to doing laboratory and clinical work at the same time while a resident at Tulane. I continued that practice during my Navy years. I did research while taking care of Navy and Marine patients. We were studying the interaction of testosterone and hostility using hypnosis. I was working with a biochemist named Harold Persky, who measured endocrine levels. Basically we were studying the effect of testosterone production rate on anger and hostility and doing behavioral correlations.

BECOMING INTERESTED IN ADDICTION

A: How did addiction come to be part of something that you pursued?

CO: During the time that I spent in the Navy, the major reason for disability was drug use—drug addiction to heroin and a lot of LSD (lysergic acid diethylamide) and alcohol. I was recruited by Dr Stunkard, Chair of Psychiatry at Penn, to begin a program for addiction at Philadelphia VA. It was natural to start a treatment program and a research program in the same place. President Nixon was running for re-election and also involved in Watergate, but no one knew it yet. He worried that he would lose the election because of the drug-addicted veterans from the Vietnam War. I wrote a proposal to the VA, which was funded as soon as I left the Navy.

A: And the rest is history. So studying addiction rose out of a practical need that you perceived for people whose lives were being torn apart by this disorder.

CO: It was then that I was reading all that I could on the science of addiction and it was very obvious that there was not much science at that time in the addiction field. For example, one of the qualifications to be an addiction counselor was that you were an ex-addict yourself, so the personal experience was like a college or Master of Social Work degree. It was obvious to me that this was crazy, so we actually did a study of the treatment results and found that the counselors we hired who had a history of addiction themselves had poorer outcomes with their patients. The Civil Service actually counted years in prison or of drug use on the street as 'education' to qualify for a Civil Service rating as a counselor. I saw a real opportunity there to apply science to this field and I began thinking of how to test Abraham Wikler's theories.

'The Civil Service actually counted years in prison or of drug use on the street as "education" to qualify for a Civil Service rating as a counselor'.

A: At what point did the idea of learned behaviors contributing to addiction come into the picture? Do you remember reading about this and thinking, 'this is interesting'?

CO: It was in the late 1960s and early 1970s. We invited Wikler to Penn to lecture a couple of times. He died soon after that time. However, in the 1970s he was thrilled that there was somebody who had access to patients who was trying to test his theory. He had observed some patients, but he did not do any experiments on patients. He had only studied rats and spinal dogs. When he died, I wrote his wife a letter explaining his influence on me and that he had been the intellectual father of my research. She wrote back a letter that I still have saying that he was very proud of my work and talked about it with her, so it was a meaningful relationship. She wrote: 'Well, he considered you his intellectual son'.

A: That is wonderful.

CO: It was so obvious to me that relapse was the important quality of addiction. I was already impressed with the proneness to relapse and somehow that meant to me that there was an engram, a memory trace in the brain. These people who keep relapsing are not being treated for the relapse mechanism in their brains. Our system pays for detox, but as you know, detox does not treat the addiction. That is not really therapy. What was really clear at that time was that spending money on setting up these big detox programs was a total waste of funds. Patients would relapse right away and so I was focused on a study of relapse from the very beginning.

A: So the huge clinical problem with addiction is that obviously you do not get it one time and then it goes away. Repeated relapse is the rule, not the exception.

CO: It sounds almost unbelievable today, but at the time people did not really think of addiction as a disease—they really considered addiction to be just bad behavior. A common belief was that antisocial personality was part of addiction and that animals could not become addicted. There was tremendous incredulity, a skepticism about animal models because it was thought that animals did not have a conscience and, because addiction was just really bad behavior, animals could not develop addiction.

A: A moral feeling.

CO: It was viewed as bad behavior rather than a disease. I was always impressed with Pavlovian phenomena as a kind of automatic non-awareness behavior. The 1970s was also a time when there were conflicts between Skinnerians and Pavlovians. Even within my own VA

service we had Don Kodleboy and John Grabowski, who were two psychologists getting into all kinds of squabbles: operant versus classical.

A: One of the questions you asked me, as part of my job interview, was what side was I on.
CO: That is right.

A: So you conceptualized an experiment to see if you could establish these responses in humans.
CO: I really wanted to see whether I could demonstrate in the laboratory the things that we were hearing from patients. I had so many stories from people saying they 'got out of Lexington', meaning the USPHS (United States Public Health Service) Hospital in Kentucky for addiction. 'When I got off the bus, subway, the train or whatever and then was back in my old neighborhood, I got sick and vomited'—you know the stories. 'I felt such craving that I immediately went out and got heroin and soon was re-addicted'—but those were just stories, and I thought that if we could demonstrate it in the laboratory and study it, we could discover new treatments. To me, this involuntary response is really the essence of what addiction is. If we do not target this, we are missing the point, so my idea was to demonstrate the creation of a new conditioned reflex that was not there before. You could establish how it developed, that they were now reacting to a previously neutral stimulus, the odor of oil of peppermint, and showing new symptoms of an addiction to opioids; so we paired the nausea and the other signs and symptoms of withdrawal with this neutral stimulus, the odor of peppermint [1–3].

A: Although you triggered the symptoms with naloxone?
CO: That is right, and I used very low doses of naloxone as an unconditioned stimulus (US). Of course, this required approval from the Institutional Review Board (IRB). There was a person on the IRB in the 1970s, a Jewish sociology professor who had survived a Nazi death camp. He was very concerned about experiments on human beings as were performed in those camps. To satisfy his concerns, he came and visited my laboratory with another committee member, a neurosurgeon, Tom Langfitt, who was chair of the IRB. I explained to them why we proposed the study and how it could help patients with addiction. I went over the conditioning hypothesis and so forth, and I said that I was going to be giving volunteer patients a very small dose of the drug. Of course, it was totally voluntary and the patient could stop the procedure at any time. I wanted to demonstrate that I could produce this new kind of conditioning in the laboratory, and he eventually bought the idea. It was not easy, but he accepted the whole idea and the experiment worked, so I remember this IRB member very well.

THE STORY OF NALTREXONE AND ALCOHOLISM

A: The story of naltrexone and alcoholism and working from animals all the way up to humans really had its roots in the late 1970s and early 1980s.
CO: That is right. I got the Investigational New Drug Application (IND) from the FDA to give naltrexone to alcoholics in 1983. Another major factor, however, was that during this time, beginning in 1971, I had the constant weight of the whole clinical program on my neck, so I was working on opioids and other drugs such as alcohol because we needed more effective treatments. One of the things that I tried that really, to this day, has never worked as well as it should was the 'one-stop shopping' idea. Comorbidity was such a huge problem and almost everybody had some kind of substance abuse plus another mental disorder—the comorbidity diagnosis—but it was really hard to get the average psychiatrist to address substance abuse and another psychiatric disorder at the same time.

'Comorbidity was such a huge problem and almost everybody had some kind of substance abuse plus another mental disorder . . .'

A: So comorbidity was an early focus for you?
CO: Yes. I was trying to develop new medications because I always thought that the combination of medication and behavior therapy was the preferred approach.

A: What you call the 'best shot' for using all the behavioral and biological tools?
CO: Animal models are a great advantage for addiction research. This led to our discovery of naltrexone for alcoholism. At the 1979 CPDD Meeting, Hal Altshuler presented his experiment where he had some monkeys who loved alcohol. Of 22 rhesus monkeys, 10 of them really loved alcohol and would work for it. He had them rigged for intravenous self-administration, not drinking, and he gave them either naltrexone or naloxone. In those days people were trying to determine the purpose of the endogenous opioid system, and blocking the receptors was a good way to explore. What he found, of course, was that 10 of the monkeys would work to obtain alcohol, but a small dose of naloxone or naltrexone would immediately reduce their intake. When their opioid receptors were blocked, they stopped taking alcohol [4,5].

A: That was an 'ah-ha' moment for you?
CO: Right. I had been using naltrexone to treat opioid addiction since 1974. Based on the Altshuler study, I decided to try it in my alcoholic patients. I applied to the

FDA for an addendum to my existing IND and I proposed a protocol to the IRB. I finally received approval in 1983. I recognized that it seemed to work well in some patients but not in others. This is where genetics comes into play. That is where I had the idea that we could pursue it in a double-blind study. I think it is really exciting right now that there is a genetic factor and that some people and some animals, when they drink alcohol, experience a big surge of endorphins which gives them stimulation and euphoria and reward. We now know that dopamine follows the endorphin release and is involved in the feeling of craving. There is much more that we know now that we did not know then, so we were sort of shooting in the dark, and I think that we were just lucky at finding that an opiate receptor antagonist blocked the good effects of alcohol.

A: So this idea of being able to look across drug classes and to try to cross-fertilize ideas, medications, interventions—that has also been an important aspect of your discovery research.

CO: The structure of the NIH actually worked against this kind of insight. People who thought of themselves as 'alcohol researchers' did not want to think that an opioid medication could be helpful in alcoholism. Alcohol research was funded by a separate institute and there was resistance to the idea that opioids were involved in alcoholism, but alcohol causes the release of endogenous opioids; so this was an idea that came before the complexities of the endogenous opioid system were known: another piece of luck. Another lucky break was that an MD/PhD student at Penn, Joe Volpicelli, came along and he was also impressed by the Altshuler data; he was studying foot-shock stress in rats. I gave him some naltrexone from the patient experiments to use in his rats. He found that in the post-stress period the rats would drink alcohol preferentially to water, unless they were put on naltrexone. Naltrexone would block the alcohol drinking.

A: Did the two of you work together at all?

CO: I took him on as a post-doctoral fellow. I was lucky because the previous fellow that I assigned to the study met tremendous resistance from the alcohol counselors. We had been duly approved by the IRB to give naltrexone to alcoholics and we had a large alcohol treatment program that had always been based on 12-Step principles. The counselors were advising the patients not to volunteer for the study. Several of the counselors were in recovery themselves, and as they did not take medication they thought the patients should not either. The previous fellow simply accepted that and very few patients volunteered for the study during his tenure. When he completed his fellowship, Joe took his place. Joe was so much better at recruiting patients and that was a key to our success. When we wanted to do a double-blind trial, I wanted to do it in our VA program. If it had not been for Joe I do not know if I could have found another person to take over the study. I could not do it myself because I was responsible for 9000 patients in the psychiatry program. I really needed somebody on the scene, and Joe turned out to be excellent, so together we got this done. Leading alcohol researchers such as Markku Linnoila could not accept the results at first. We received some really nasty reviews on papers and on grant applications. Later, after our results were replicated, Markku became a strong supporter. He and I were both at a Nobel Symposium in Stockholm in the early 1990s and we flew back to the States together as seatmates. During the flight, he said: 'You know, I really have to apologize to you. You discovered something very, very important. You should be very proud. You must feel really great about this'; and he said: 'I realize that I was wrong'. For me, it was a very nice experience because I respected him as a scientist. He later died at a young age of cancer.

A: Right.

CO: When I was a resident I remember that lithium was first being used in psychiatry and we used to spend a great deal of time trying to determine whether someone had schizophrenia, particularly schizoaffective schizophrenia versus manic depressive illness, which we now call bipolar disorder. After a conference with a patient interview, we might say: 'Well let's see. It sounded to me like loose associations'; 'no, it was flight of ideas'.

A: Splitting of hairs and language; so as brain imaging tools have become available in the last 15 years, your interest in taking a peek inside the brain to see what was going on during these conditioned responses must have resurfaced.

CO: Yes, our early imaging research with Hank Kung was very exciting. It fit right in with the cue exposure research that we began in the 1970s [6,7]. We now know so much more about the reward system, and this is what determines whether a given drug will be abused. People like it when the reward system is activated. It does not matter whether it is from cocaine, alcohol, opioids for pain or even gambling. That is why, in DSM-5, we added gambling to the list of addictions.

A: You could show activation of the reward system when the patients reported craving. The more recent studies that you did with Nora Volkow showed very well that when people are craving, there is a release of dopamine and that the intensity of the craving correlates extremely well with the amount of dopamine released.

CO: That is one of the reasons we added craving to the list of symptoms for DSM-5. It may be the only psychiatric symptom for which we already have a physiological basis.

A: The brain imaging translation research began in the early 1990s as a direct translation from conditioning theories?
CO: Yes, the dream was to find behavioral treatments, possibly extinction, that could suppress this learned response, or medications that could suppress. As you know, some 'anti-craving' medications have shown promise and we are still working actively on this.

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A: What has been the biggest frustration in your research?
CO: When I look at treatment programs around the country, I find that evidence-based treatments are not generally used. Most programs are still delivering the same methods that began in the 1960s and 1970s. There has been a great deal of progress in developing new medications, but only a minority of patients receives them.

A: Resistance is something that, even when the science is good and even when the clinical science is strong, taking it to the next step has been a challenge at times. Conversely, some big gratifications—being able to see a medication go all the way from an animal model, such as with naltrexone and alcoholism, all the way to the clinic, and even to have the heterogeneities explained by genetics—has to be pretty gratifying.
CO: That is really good if it were only applied more extensively. The pharmacogenetic approach should be applied in all areas of medication. In our alcoholism work, we were lucky to discover an allelic variant that signaled what is probably a biological subtype of alcoholism. I truly believe that, in the future, physicians will acquire the patient's genotype and then select a medication based on genotype [8].

A: You have some colleagues with whom you have interacted and who stimulated research paths, exchange of ideas, such as George Woody and Tom McLellan. Would you like to say a few words about them?
CO: George came from a non-research residency program, but he was really interested in addiction and interested in becoming an academic. He developed into not just a really superb clinician, but also one who learned how to design clinical trials. He initially played a supporting role, and then he became an independent investigator. It was a beautiful trajectory. Tom McLellan is just one of the smartest people I have ever met, and he is extremely well organized and energetic. He is a hard worker who is serious about everything and accomplishes a great deal. When he arrived in the late 1970s we were working with Jim Mintz on a measure of addiction severity. When Jim left, Tom took over the project, which became the Addiction Severity Index.

A: Tom had the practical side—a gift for looking for a practical niche, a need to get things done.
CO: Then there was Anna Rose Childress, bringing such creativity and dynamism. There are so many people that I could say nice things about. All our research has been a team effort. On a more clinical note, there are Bob Greenstein and Jim Cornish, and Arthur Alterman did some really good research in our group. Then more recently there is Helen Pettinati, Kyle Kampman and Teri Franklin. We also have some happy and exciting memories to share. The visit by President George H. W. Bush in 1991 was a landmark. No other VA or any other treatment program had been honored by a visit from a sitting President with hordes of reporters and TV cameras. The stated purpose was to demonstrate that treatment of addiction can be successful, a major point of the President's program.

A: Being able to overlay the genetics with the brain response?
CO: That is the next chapter, I think, in terms of basically understanding the heterogeneity of addiction patients. We now look at heterogeneity of the treatment response. With alcoholics, you have the genetics of the opioid response to alcohol and underlying that clinical response is the brain, so we are unraveling the complexity by characterizing patients by genetics and brain response.

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COMMITMENT TO TRAINING

A: One of the extraordinary legacies that you have, in addition to the scientific findings and being a general ambassador for addiction as a disorder with important brain underpinnings, is training students—getting that message to the next generation of clinicians and scientists.

CO: Well, I think that one of the most serious problems in this field is that there are so few physicians who know anything about addiction. I think the knowledge gap is huge. Study of addiction should begin early in training, because addiction is one of the most common disorders in all of medicine. It should be part of all medical school curricula. As far as I know, the course that we have at Penn is the only full course on addiction that is required; it is not an elective. I feel that course is very important and I got it into the curriculum because of the good sense of students. From 1971 until 1989 we had an elective course plus a few lectures here and there in pharmacology and psychiatry. In 1989 we had a retreat where the faculty met with students and recent graduates and we asked the graduates what they did not learn in medical school, but they wished that they had. There were a lot of interesting responses about treatment of congestive heart failure but they almost unanimously said: 'most of the patients we see have substance abuse of some kind. Unless we took Dr CO's elective, we did not learn anything about it'. I immediately said: 'I will be glad to teach a full course'. I got it into the curriculum because at that time the curriculum was being reshuffled. Since 1989, all 160 students each year have taken the required course. The students have given the course high scores and several teaching awards.

A: You have probably one of the best bird's eye views of this field in terms of its evolution about what addiction is. You mentioned early on that people viewed addiction largely as a moral failing, willful misbehavior, and gradually the brain sciences came to the front—could you say a little about that trajectory, about the progress you have seen in the way addiction is viewed and the places where we still need progress?

CO: First of all, it was completely neglected by organized medicine and it is still largely neglected. There have been patients, even in psychiatric therapy, whose doctors did not want them to talk about the drinking, because that is just not really the 'core problem'; but those of us in the field know better now. It has also changed in terms of what addiction is. You hardly ever hear anymore of people talking about it as some kind of moral failing; however, in a way we still treat it that way because in the health-care system in the United States, addictive disorders do not have full parity with other genetic diseases. There has been progress, and the Affordable Health Care Act ('Obama Care') will make a huge difference. It will actually save money for the health-care system. I think the biggest continuing problem in this regard is that people, even health-care providers, have a tendency to feel that the addict brought it on himself. They should just say 'no' when offered drugs, and addicts are really to blame for their problems. My position is that most people who make the mistake—make the bad choice of trying drugs—do not become addicted. Only 16% of cocaine users eventually develop addiction, so those who are unlucky enough to have the genetic make-up for addiction are the ones that become hooked and, once hooked, they might as well have diabetes or hypertension. Therefore, it makes perfect sense to cover addiction in a national health plan.

A: You mentioned that in the early years there was great resistance in the treatment community to any medication for addiction. Have you seen an evolution in the traditional treatment communities regarding their acceptance of medical treatment?

CO: Yes, I am hearing positive reports; but there was a recent CNN special program on addiction that followed five patients over a year through their addiction, mainly alcohol and cocaine, and they all went to really famous programs such as Hazelden or Betty Ford and they kept relapsing. They were interviewed on admission, at the end of treatment, and then again when they each relapsed. The entire series is on the CNN website. At graduation, they would say: 'This time I'm really gonna stay off. I'm never going to relapse'. Yet they all relapsed. In a later scene, Dr Sanjay Gupta showed a successful naltrexone patient interview to the staff of these famous programs and he asked the head of counseling at one of these programs: 'What do you think about this?'. This counselor responded: 'You know, I don't believe in that. It's just a crutch. You have to really work the program'. This is amazing.

A: Therefore, after all these years of science, it still has not penetrated far.

CO: I do not want to end this on a negative note. We have made a great deal of progress in understanding addiction, in discovering new treatments that are often very effective, but not always. Nevertheless, there is still resistance to biological treatments among the majority of therapists in the United States. We hope that health-care reform will further the progress of biological treatments. Primary care doctors will be paid to identify early cases and to treat them like other chronic diseases. I am optimistic about the future.

'We have made a great deal of progress in understanding addiction, in discovering new treatments that are often very effective, but not always. Nevertheless, there is still resistance to biological treatments among the majority of therapists in the United States'.

A: What advice would you give to younger scientists who are just starting out?
CO: Stay in touch with patients as well as research, find a good role model or mentor, try to have a balanced life and do not forget about family responsibilities; divorce is a major impediment to a research career.

A: One final question, of a more personal nature: when you are not occupied with research and administrative duties, what do you do to relax?
CO: I am an avid skier, 'addicted to skiing' especially in the Alps, a regular enthusiastic tennis player, love the French language, and like to lecture on science in French. I have just been chosen for a French 'knighthood' (Chevalier dans l'Ordre National de la Légion d'Honneur).

Note

The opinions expressed in this interview reflect the views of the interviewee and are not meant to represent the opinions or official positions of any institution or organization the interviewee serves or has served.

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