

## **Barney Carroll Conflicting Interests**

### **When did you come into contact with Charlie Nemeroff?**

I moved to Duke from Michigan in 1983. Charlie Nemeroff and Peter Loosen were at UNC Chapel Hill, and they made contact with me very early. I wanted to get a mood disorders program up and running - I would not be able to be hands on as Chair. There were just too many other demands, so I needed to get good faculty to gear up a mood disorders program. Duke had Jonathan Davidson at the VA hospital but, at least at that time, he was not keen on moving across to Duke proper. It was a different salary structure, and so Jonathan stayed where he was. The other mood disorders investigator already present was Bill Zung, of the Zung Rating Scale fame, but Bill was already ill with cancer from which he died in around '88. So Bill was not the person to develop a program.

Peter Loosen was someone I already knew. In fact we had talked with him about moving to Michigan a few years before, and when I came down to Duke he and Charlie Nemeroff contacted me to see were there any prospects for them at Duke. I thought to myself 'well this is a stroke of good luck' because Peter would be able to head up the program. Charlie came along in a secondary role, and a third person was Garth Bissette, their laboratory person. So that's how I brought them in, in '84. Unfortunately things didn't work out the way I hoped. Peter's performance in developing research funding and momentum led me to remove him as chief of the program in 1985. I did not put Nemeroff in charge. One reason was that I felt he lacked administrative experience and aptitude. I put in Dan Blazer, because Dan at that point was winding down his major role with the ECA programme and he had a clear national presence in geriatric depression. So I put Dan in charge of the mood disorders program. Charlie stayed in the program as an attending, and he had laboratory space as well, and he walked between the two just as I had walked between the two in my days at Michigan. By the 'between the two' I mean the clinical setting and the laboratory setting. The other key member of the mood disorders group was Ranga Krishnan, who had support from my NIH grant. Nemeroff did succeed at obtaining grant and foundations funding for his laboratory work, where Garth Bissette ran things.

### **What was your view of Charlie then?**

Well, it became apparent that Charlie needed a lot of oversight and a certain amount of hand-holding. He was young, inexperienced, brash, with a sense of entitlement and narcissism. I recall one time he had a grant proposal turned down – he was crushed, psychologically. I needed to go over to his office in the laboratory building and sit with him for an hour, to console him and help him process the narcissistic blow. But that was OK – that is one of the roles of a chairman.

Nemeroff's style raised lots of eyebrows. I found myself frankly running interference for him on a few occasions with the administration of the medical school. There were times when I had to call him into my office and administratively box him around the ears. I won't go into specific events, but

there were several times that I needed to do that. Early on, I cut him a good deal of slack because I hoped that I could shape his behaviour and be a role model to him of a professional and principled academic investigator. He was not at that time deeply involved with drug companies, but he certainly was heading in that direction. One his characteristics was a penchant for gossip. I used to say jokingly to other faculty - you know Nemeroff is the most gregarious academic person I have ever met - meaning he hangs out on every street corner trading gossip. That tendency to gossip and rumour mongering has proven to be malignant over the years, and became a real problem. I will give one example: Nemeroff telephoned me one time to let me know he had confidential information that my NIH grant application was going to be funded. He passed this privileged information to me with the clear intent of ingratiating himself. My reaction was to chastise him for failing to respect the confidentiality of the information, no matter how he obtained it, and for trading on this insider information to inveigle his way into my good graces (I was his chairman, after all). I reminded him that I was getting NIH grants when he was still in knee pants, that I didn't need him looking out for me, and that I was not losing any sleep waiting for the official notice of award.

**Could you envisage at that point in time Charlie being the force that he later became?**

Not until later. By the time I was leaving the Chair in 1990, he was becoming more and more flagrant in his narcissism, grandiosity and entitlement. His deep involvement with the pharmaceutical companies really began maybe in 1991 at Duke but even more so after he moved to Emory.

**Do you think his role in helping defend Prozac in 1991 was the event that helped bring him to national prominence?**

I think that was a signal event, yes. He performed at the FDA hearings on the potential suicide risk of Prozac. He was completely unqualified to discuss the matter because, to this day, he doesn't understand epidemiology and risk-benefit assessments in clinical pharmacology. But he was prepared to go in there and be a blowhard. That was noticed by everybody. The drug companies curried favour with him subsequently.

In terms of expertise, the depth of Nemeroff's science in many areas is quite shallow. He's got a kind of hit and run style in research. He'll climb on to some current bandwagon, do a few things with it and then move on to something else. One of the characteristics, as I look at his research output, is how fragmented it has been and how there has not been a great deal of follow through thematically over the years. For instance the work on CRF in cerebral spinal fluid came out in 1984 or '85, and basically, even in that work, like most of what he does, his role was the research broker - the samples came from Eric Widerlov, the assays were done by Garth Bissette, the statistical analyses were done by someone else, and the glory was taken by Charlie, who had really not contributed any primary data or effort or quality control oversight. All he did was to schmooze with Wylie Vale to obtain the reagents needed for the assays. The person who should have gotten the credit for the work was Eric Widerlov in Sweden. But Charlie made sure that he took the major credit, and that has been the story of his career ever since.

He also was constantly grooming others, with the expectation of reciprocity later. I recall asking him why Peter Loosen was included as an author on the CSF CRF paper in Science. Charlie gave me a crooked smile and admitted he gave Peter honorary authorship – it cost Charlie nothing to do so, and it put Peter in his debt.

As an example of failed follow-through, Nemeroff has never systematically pursued important questions about the CSF CRF story, like whether the purported elevation is seen in melancholic cases or other clinical subtypes, or in refractory depression or psychotic depression or bipolar disorder. His work on change with treatment is very sparse, and what changes he did report may well just represent regression to the mean, for all we know.

Back in 1991 we were coming up on the World Federation of Societies of Biological Psychiatry conference in Florence, Italy. I was the assistant secretary of WFSBP, thanks to the efforts of Charlie Shagass, who was the Vice President of the organisation. I found myself a member of the jury for a research award. Nemeroff sent in a submission, and I recognised immediately that of the three research publications he had submitted, his role in two of them was very minor. He was more or less an honorary author on these papers – something he is skilled at arranging. I also knew that Nemeroff most likely had not informed the faculty persons who did the real work that he was using these publications to get an award for himself.

So I made an issue of it, and the upshot was that one of the faculty members whose work he had basically expropriated insisted that that paper be withdrawn. The other faculty member was disturbed but declined to insist on withdrawal of the paper. He later moved to Emory with Nemeroff. By the time we realised all this it was too late to prevent the award going to Charlie. I well remember sitting at the event in Florence with Charlie Shagass next to me, and when Nemeroff came up to get his award Charlie Shagass leaned across and said this really tarnishes the whole thing. That incident was fairly typical of Nemeroff's behaviour.

### **He seemed to have been good at doing deals.**

Yes. One series of events illustrates this, and the low level to which the field has descended. There was a very well regarded publication called Psychopharmacology Bulletin that began in the 1970s or maybe even the 1960s. It was produced by the Psychopharmacology Research Branch of NIMH, and it was a vehicle for various conference abstracts and research reports. It was totally non-commercial. Robert Prien was the editor.

Fast forward to the 1990s, when Steven Hyman came in as the new Director of NIMH. Hyman was a brash young person who came out of Yale and announced that from now on NIMH would be focussed on translational research, and that priorities would change. One of the fallouts was that the Psychopharmacology Research Branch was abandoned and the Bulletin was no longer funded.

At that point a publishing entrepreneur in Los Angeles named James La Rossa obtained the rights to the journal title 'Psychopharmacology Bulletin'. He engaged Nemeroff to edit the new journal. We don't know how much La Rossa paid him. Nemeroff proceeded to transform what was a genuine academic publication into the scientific equivalent of yellow journalism, with supplements funded by pharmaceutical companies, filled with infomercials that in turn had been written by ghost writers, and for which the academics received back door payments from the drug companies. These payments were laundered as "unrestricted educational grants" from the drug companies. In fact, I have one of these in front of me right now, Spring 2003, an entire supplement on Paxil funded by GlaxoSmithKline and organized by Nemeroff, in which one of the notorious articles by Zachary Stowe appears as well as one by Nemeroff himself.

Now, in 2002 Nemeroff became editor of Neuropsychopharmacology. In that role he was obliged to relinquish his other editorial commitments. The editorship of Psychopharmacology Bulletin went to Michael Thase. But in return for giving up Psychopharmacology Bulletin and some other things Nemeroff struck a deal with the publications committee and with council of ACNP. The deal was that in compensation for what he was giving up they would pay him \$50,000 a year to edit Neuropsychopharmacology.

**For the most part these posts are unpaid aren't they?**

I think some editors, like Chris Gillin, Chris Fibiger, and Herb Meltzer may have received some nominal support to help them with office staff or something like that, but a payment to the tune of \$50,000 really raised eyebrows. Even more so because ACNP council did not make a public announcement of it. And of course the selection committee for the editorship was stacked – chief among them was Dennis Charney who is a well known crony of Nemeroff.

**When did things begin to come to a head between you and Charlie?**

Well, after Charlie left Duke in 1991 I more or less forgot about him. We had very little contact, and that suited me fine. I had no reason to make life difficult for him. I was just happy to see the last of him at Duke. I think he blames me for the fact that he did not get the chair in psychiatry at Duke, which he badly wanted. Allen Frances came in as chair, so Charlie had to settle for Emory. I did hear from many people around that time that Charlie was badmouthing me to anyone who would listen. As for the Duke chair, I know from discussions I had at the highest levels that Nemeroff never had a prayer of getting that prestigious position. I didn't need to do anything to block him from getting it.

Some people, instigated by Nemeroff, have accused me of being on a vendetta against Charlie, but that's not true. I would say from '91 until 2002 I basically ignored him. I was certainly not pursuing him. And those who say I am on a vendetta will need to explain what Charlie was supposed to have done to me that would have given me any such motive. Aside from my exasperation with his behaviour and character, there was no way for Nemeroff to affect my equanimity. I was his chairman, for heaven's sake, and I worked very hard to promote his career and to teach him good scientific values.

When he was appointed editor of the journal at ACNP I bestirred myself to send a warning to ACNP council that they were making a big mistake. That warning was based on the number of Nemeroff's conflicts of interest, which were well known by the time he was appointed. Of course, ACNP were in no mood to listen. They went ahead and confirmed his appointment as editor, and they have lived to regret that decision.

Later on, I began to notice in the journal that he was engaging in self dealing and academic nepotism. It's very easy to check this. I went to Medline and looked at the number of publications he had in Neuropsychopharmacology for the years before his appointment and then the years after his appointment. His rate of publishing his own stuff in NPP went up over 4-fold after he became editor, from something like 4% of his total publications to something over 16%. In addition, I could read between the lines and see that he was sponsoring his own faculty, his own trainees, his own friends and his own corporate clients with publications and product placements in the journal as well. So I sent a letter to the Council saying look you've just got to keep an eye on this guy.

There were a couple of minor interactions over things like editorial issues with the journal, and letters to editors about one or another of Nemeroff's problematic publications. In typical fashion, Nemeroff displayed hypersensitivity to even normal scientific criticism. You could always count on him to respond in an ad hominem way rather than professionally. That is a trait he has passed on, sadly, to several of his junior faculty associates at Emory.

But the real public confrontation with Nemeroff did not come until 2003. In late 2002 he published a review article in Nature Neuroscience, an overview of treatments of depression. As I looked through the published article I saw several very clear instances of undeclared conflicts of interest. One was a reference to a lithium delivery patch on which he held a patent. That was not disclosed. Second, he wrote in unwarranted positive terms about Corcept's drug RU486 for the treatment of psychotic depression, without disclosing that he was a member of Corcept's advisory board and a stockholder. And then third, he talked up, again in unwarranted positive terms, a drug called milnacipran, which was really a dud antidepressant that a company called Cypress Biosciences was attempting to resuscitate for fibromyalgia. When I saw that in the article, with an explicit branding mention of the company's name, it took 5 minutes on the Internet to establish that Nemeroff was advising Cypress Biosciences, and that in fact he had an incentive performance contract with them, so that if the drug reached certain clinical milestones they would pay him extra to the tune of I think \$100,000. So he slipped some publicity for the company and for the drug into his review article, without disclosure.

I discussed this with Bob Rubin, a long time colleague, and Bob and I decided to get in touch with the editors at Nature Neuroscience. To make a long story short, from February 2003 through the middle of July 2003, four and half

months, Bob and I had exchanges with the Nature Publishing Group, involving eventually Philip Campbell, the editor of Nature proper, and in a word they stonewalled us. They didn't want to hear about it. They threw up all kinds of chaff and distractors and technical legalisms in an attempt to make us drop it and go away. Basically Nature's position at the time was 'we are Nature, we make the rules, whatever we decide is what's right, and we have decided that we don't need disclosures for our review articles, only for original research submissions'.

Bob and I were not about to go away, and after four and a half months of this stonewalling we said let's go public with this. You know, you start off working through normal professional channels, and when you meet stonewalling eventually you go outside channels. By late July we had made contact with a journalist, Melody Petersen at the New York Times, and Melody said to Bob 'I'm going to run with this', and she did. It hit the street in the New York Times August 3, 2003, and quickly become an international cause célèbre. It sent Nemeroff running for cover, pointing fingers all the way. It sent Nature running for cover, and eventually led to them agreeing to publish the letter we had originally sent, along with a reply from Nemeroff, which was a disgraceful piece of ad hominem smearing and evasiveness. It led also to the entire Nature Publishing Group re-evaluating and changing their policies on disclosure - an outcome that Bob and I thought was very good.

We weren't pursuing this to harass Nemeroff. We were pursuing it because it was something that the field required, and once that was done it was done. It was, as I say, an international scandal. But things quietened down, and Bob and I had very little else to do with Nemeroff until three years later. Nemeroff has said we've been harassing him. He's said it in e-mails to his own Dean at Emory, that showed up in the material that Senator Grassley released. Fact is we were not harassing him - we were simply trying to do what was right for the field. I really didn't care what Nemeroff did down at Emory, as long as he was not damaging the image of our field.

So that brings us to July 2006, when in Nemeroff's own journal, *Neuropsychopharmacology*, we saw yet another flagrant example of self dealing and lack of disclosure. That of course was the infamous vagus nerve stimulation (VNS) review article authored by Nemeroff and seven co-authors, six of whom were members of the advisory committee to Cyberonics, the company producing the vagus nerve stimulator. The relationship of Nemeroff and these other academic authors to the company was concealed. The last author was an employee at Cyberonics, which was acknowledged. In addition there was a euphemistic reference to 'editorial assistance' by a person called Sally Laden - that's a euphemism for 'she wrote the paper'. She later clarified that she was paid by Cyberonics to write the first draft, being careful to stay 'on message,' then she released it to the "authors." Their contribution was to strengthen the hard science surrounding the stealth infomercial.

In July of '06 then, we alerted the ACNP, and their response was to ignore us. We literally got no response at all. Mind you at the same time that this was going on, Bob Rubin and I were enmeshed in other issues with ACNP, which

were the ethics complaint brought against us by the Corcept people, and a nasty conflict about defamatory material posted by Schatzberg on the ACNP website. Also, on July 10, 2006 the article about Corcept by Paul Jacobs appeared in the San Jose Mercury News. So, there was a lot of fur flying right around this same time when the VNS issue broke.

Actually, back in July-August 2006 Israel had its conflict with Lebanon to the north and Gaza to the south, and Bob and I joked that we were like Israel – at war on two fronts simultaneously. After about a week, having heard nothing from ACNP in response to our concerns about the VNS publication, we conferred. Bob and I decided ‘look if they want to stonewall that’s their business, but we’re not going to sit around on our hands for another four and half months like Nature subjected us to’. So we took the material we had given ACNP, made some appropriate editorial changes, and sent it to David Armstrong at the Wall Street Journal, who was delighted to receive it. He broke the story July 18, 2006. It was then picked up by the New York Times, with further stories and editorials. The New York Times editorial called Nemeroff’s self dealing “incestuous.”

The VNS affair also became an international cause célèbre. And we now know from internal e-mails at Emory that it was a mortal blow to Nemeroff. That was the beginning of the end for his standing within his own institution. ACNP eventually published a delicately phrased corrigendum to the article, acknowledging the conflicts of interest of the authors. ACNP Council were pretty angry with us, but we just told them ‘look we gave you your chance, you didn’t do the right thing, now you need to live with it.’ The fallout from the VNS issue continues to this day. It’s something that still reverberates around the system. It led the field as a whole to focus again on conflict of interest issues. I mass e-mailed my friends and ACNP members over July and August, bringing a lot of pressure on ACNP council, and I think they were taken aback by the negative feedback coming from the field.

Their original position was that mistakes were made, procedures needed to be tightened up, but there was no decision to remove Nemeroff as editor. That was the situation the first week of August. But a short time after that, in response to the feedback coming from the field, the ACNP president, Kenneth Davis must have persuaded Nemeroff that he had to go, and it seems he allowed Nemeroff to save face by announcing that he was stepping down because the controversy was not good for the journal. At the same time, Nemeroff could not bring himself to acknowledge any error or wrong doing of his own. That was fine with Bob and me – the main thing was to get Nemeroff out of that editor’s job, because he had thoroughly corrupted the journal.

An amusing after shock from the VNS event was that a group of Nemeroff’s trainees, faculty members answerable to him, and a few friends from around the country wrote a letter of protest to the Wall Street Journal defending Nemeroff and repeating Nemeroff’s self serving smear that the fault lay with the administrative staff of the journal. Bob and I saw this and we immediately jumped on it. With David Armstrong’s help, we published a reply which basically cut Nemeroff’s supporters off at the knees. We called their letter an

insufferable smear on the ACNP staffers. To this day, whenever one of those signers of the protest letter opines about ethics or tries to defend Nemeroff, I remind them of their complicity in that ill-advised letter to WSJ. There were some surprising people who did sign that letter – Robert Golden, who is the Dean of Medicine at University of Wisconsin, Madison; Jeffrey Lieberman, the Chairman of Psychiatry at Columbia; Martin Keller, who was Chairman of Psychiatry at Brown; Ned Kalin, the chair of psychiatry at UW Madison; and Michael Davis, a member of ACNP Council.

These were the two events that brought me and Nemeroff into public conflict. But as I say they were not driven by any kind of campaign, much less a vendetta against Nemeroff, which is the smear that he puts around. They were in response to his flagrant, recidivist violations of ethical standards.

The more recent round of troubles Nemeroff has had, beginning in October '08 when he was outed by Senator Grassley, had nothing to do with me or Bob Rubin. We read about it in the newspaper just like everybody else. We were subsequently contacted by staff in the Senator's office and we did dialogue with them, helping them to understand some of the materials they had obtained, but I let it be known immediately to ACNP council and to others that Bob and I had absolutely no role in Senator Grassley's decision to investigate Nemeroff. I don't know who did.

I was going through some old mail recently and I came across a message from Paul Jacobs, the journalist at the San Jose Mercury News who did the piece exposing Schatzberg's exaggerated claims for his RU486. This was an e-mail message from Paul Jacobs in early '07, six months after the newspaper story ran, asking me had we been contacted by Grassley because something might be developing in that direction. And I wrote him back and said 'no we haven't,' and we weren't contacted, right up to the time when Grassley's exposé of Nemeroff hit the streets.

### **Can I take you to the Corcept story? What are your links to Alan Schatzberg?**

Alan Schatzberg and I had been friends for many years. I must have crossed paths with him first in the late '70s at venues like Biological Psychiatry meetings. He was in Boston then. He's an affable chap. We never had much substantive interaction on projects, although I did supply him with blood samples from my endocrine project at Duke in order to help with one of his grants. But my role was just to ship him the blood samples, and I really had no part in what he did with them, much less any publication that came out of them. So basically my relationship with Alan just was one of comfortable professional friendship over many years.

When I came out here to Carmel, which is just 90 miles from Stanford, where he was by then, I got in touch with him and I visited several times. He arranged for a courtesy faculty title of Consulting Professor in the Stanford department, and he asked me to help him with preparation of a grant renewal, which I did. He wrote me in as a \$10,000 a year consultant on his grant, which



was funded, and the deal was that I would go there from time to time to meet with him and talk science, and give him advice as needed from a distance.

It was a comfortable relationship until late 2002, when I saw his report on his drug in the journal *Biological Psychiatry*. I immediately recognised it as problematic. They reported on the use of their drug called RU486, which is a cortisol and progesterone receptor blocking agent. The design of the study was to treat patients with psychotic depression. The theory was that elevated cortisol in psychotic depression may be causing the psychosis, therefore a cortisol receptor blocker may be helpful.

There is a little bit of clinical evidence to suggest that this theory was not completely far fetched. For instance, the psychosis in patients with Cushing's disease responds quite well to treatment with RU486, although you have to realise that the magnitude of cortisol hypersecretion in psychotic depression usually does not overlap with the degree that is seen in Cushing's disease. So that was the rationale for the study, but when I looked at the report it was very clear that they were making a silk purse out of a sow's ear. A major problem was that they did not present any statistical analyses on clinical outcome. One of the 3 doses was a very low dose of RU486 that served as a so-called active placebo. It was very clear that there was no significant difference between the two high doses of the drug and the active placebo. But in the published report they presented no statistical analyses of outcome, and yet they injected a very optimistic tone about effectiveness into the report. They even issued a Stanford press release in which Alan Schatzberg stated giddily that RU486 may be the equivalent of ECT in a pill.

Even worse, the article was published as a so-called 'priority communication'. The person who made that decision was Dennis Charney, the editor of *Biological Psychiatry*. The publication of Schatzberg's report was accompanied by an editorial written by Dennis Charney. Charney had two co-authors for his editorial. One was Philip Gold, who I think did the heavy lifting in writing the endocrine aspects of the report. The second was Wayne Drevets, whom I regard to this day as an innocent bystander in this whole affair. His name was put on the editorial because Phil Gold wanted to use some of Wayne's imaging data to make a psycho-endocrine point. Charney was chief of the intramural program where Gold and Drevets worked, but as far as I could tell there was nothing substantive that he had contributed. Nevertheless his name was on it, so he owns it to this day. Charney also had fronted for Corcept several times in the preceding year, in a *New York Times* interview, and in a lecture to NARSAD, where he talked up Schatzberg's drug.

Well, again, I discussed this issue with Bob Rubin, and we contacted the journal in Dec 2002. They got some reviews that said that the journal should publish it and others that disagreed. But the main reason that our letter was never published was that the journal received an abject response from Schatzberg, that did not rise to the level of a scientific response. It was primarily an ad hominem attack on us, with statements to the effect 'don't these people have anything better to do than sit around and nit pick about our publication'. The journal fell back on the policy that the *entire package* needed

to be publishable. As the Schatzberg was clearly substandard, they decided to deep six our letter as well.

So then there was a back and forth. I had tried to be collegial about this, even though we were coming down very hard on them about the poor quality of the science. At the time we sent the letter off to the journal, I sent a cover letter and a heads up copy of the letter to Schatzberg himself, emphasising that this was a matter of science and not of personal attack. I copied this to Dennis Charney. Neither of them acknowledged receipt of my attempt to be collegial.

When we got their very biased and ad hominem response eventually, Bob and I revised our letter, shortened it, toned it down, sent it back, and Eric Nestler, the editor who was subbing for Charney, rejected our revised letter forthwith. He rejected it the day he got it. And for me that was the end of it, except I followed up after a few weeks with a 'lessons learned' communication to everybody who had been involved - Schatzberg, Charney and Phil Gold. And that was about the end of it.

Of course right around this time the Nature Neuroscience thing was cresting and I needed coronary bypass surgery. I ended up in the hospital at UCLA, and Bob Rubin who was then still at Pittsburgh handled things for a month or two until I was back on my feet.

That takes us then to the next main episode in late 2004 at the ACNP conference, when Bob and I presented a poster discussing Corcept's published results, commenting on how weak the science was. At the same time we pointed out the conflict of interest involving the Corcept principals, Schatzberg and Belanoff, and also some members of their advisory board who had been touting the drug in other scientific publications and media interviews, including Nemeroff and Bruce McEwen.

This poster went up at the ACNP meeting and drew a great deal of attention – some of it amused, some of it furious. People took a very partisan view of what we had done. Many people said 'good for you guys – it's about time somebody called out these people on their conflicts of interest.' Basically, all we did was to highlight how weak the science was, to quote testimonials that the individuals associated with the company had published, and to juxtapose those testimonials against their known financial involvement with the company. People drew their own conclusions as to what to make of this.

But that evening there were also a lot of very angry cronies of Schatzberg wandering around with frowns on their faces. And a few weeks after the meeting we were hit with a complaint to the ACNP ethics committee, which turned into a major harassment that dragged on for almost a year. In the process of responding to these charges, we discovered that the internal processes of ACNP are inquisitorial, non-transparent, lacking in due process, arbitrary, and capricious. We were forced to become parliamentarians, to really scrutinise the bylaws of the organisation and to challenge whether the complaints were consistent with what the bylaws provided. In fact they were not.

The complaints that Schatzberg raised, in a very heated letter to ACNP's secretary, Oakley Ray, were essentially scientific disagreements. His position was, if these people disagree with my science, that's unethical. Oakley Ray should have known better and should have understood that Schatzberg's complaints were inconsistent with ACNP bylaws. However Oakley Ray was not disposed to act accordingly, because Bob and I had outed him internally to the college for misappropriating college personnel to work in his own private business. This never got out into the general public, but there was a letter of record sent to him by the President at the time, and Oakley was still kind of smarting from that. He knew Bob and I were the ones who had called him on it. So when Schatzberg's complaint came in, Oakley was not at all motivated to look at it carefully and to screen out what was garbage from what was a substantive ethics issue. There was no substantive ethics issue. It became clear over time that Schatzberg wanted to use the secret ACNP ethics committee process as a means of shutting down scientific criticism of his clinical trials and his company, Corcept Therapeutics.

We went through 11 months of harassment, first by the ethics committee and then by council, with the attorney for ACNP having an extraordinarily prominent role in the proceedings. It turned out that ACNP officers wouldn't put pen to paper without the attorney essentially drafting it for them. And he did a terrible job.

The upshot of all of this was that the ethics committee did not support any of the complaints raised by Schatzberg. But the committee then turned around and invented a new charge, which Schatzberg had not himself raised, namely that we had made personal attacks on Schatzberg, and other members of the College, and that we had not signalled in our abstract for the poster that it would contain this material. That part was correct, because the bit about juxtaposing the testimonials with the conflicts was a last minute add-in to the poster.

As to the personal attacks we were supposed to have made, we challenged the ethics committee Chair, David Rubinow, and later challenged the ACNP President at the time, Daniel Weinberger (a friend of Nemeroff and Schatzberg), and we challenged later presidents, Kenneth Davis and William Carpenter, to cite verbatim from our poster what was a personal attack. None of them had the integrity to respond to our challenge, and it is still our position that there was no personal attack. We juxtaposed the information and let people draw their own conclusion about whether the exaggerated testimonials like 'ECT in a pill' were influenced by the largely undisclosed financial conflicts. Finally, we received a confidential letter of admonishment from ACNP council.

### **How long did it take to we get to this point?**

Eleven months. We were told that all proceedings of the ethics committee and council in this matter are strictly confidential and may not be disclosed. A month later I was renewing my medical licence, and one of the questions on the renewal form was 'Have you been sanctioned by any professional body

since your last renewal of the licence?’ So, I contacted our attorney and his advice was ‘yes you have been sanctioned and you are obliged to report this’. So, I informed ACNP that, despite their position that none of this information should be released, I was obliged to report it to the North Carolina Medical Board, and if ACNP had a problem with that - too bad. I got no response to that communication.

This takes us to late '05. On July 10, 2006, Paul Jacobs' article comes out in the San Jose Mercury News, with input from us, and does a devastating job picking apart Schatzberg's claims. Paul Jacobs is an investigative journalist; he ran a two part series – one on Stanford Medical School as a whole and then the second part was devoted entirely to the case of Dr Schatzberg and Corcept and the claims made for their drug.

Meanwhile, in February 2006 Bob and I sent a letter to the editor of Neuropsychopharmacology, critiquing a new article by Schatzberg that appeared online in September 2005, and in print in 2006. A letter of response was received by the journal from Dr. Schatzberg. Both letters were posted on the ACNP website June 21, 2006. The response from Schatzberg was defamatory, and we asked ACNP to take it down. They refused. We consulted our attorney, who demanded a retraction and removal of the offensive material, with a warning of potential legal action. The defamatory material remained on the ACNP website. The NPP field editor responsible for the decision to post the offensive letter from Schatzberg was Raquel Gur. Through our attorney we informed the publisher, Nature Publishing Group, of our concerns. The attorneys for NPG had no control over the ACNP website, but they did require Dr. Schatzberg to remove the offensive material before his letter appeared in print in December 2006. In this case, the attorneys for NPG displayed a better appreciation of the ethical issue and a more principled posture than did the attorney for ACNP or the officers of ACNP.

In May 2006, about 8 weeks before Paul Jacobs' article appeared, we received an extraordinary communication from ACNP saying in effect, ‘Dear Dr Carroll, Dear Dr Rubin, it has come to our attention that you are in discussions with a journalist, and we require you to inform us when, how, under what circumstances, and what was discussed’. We wrote back and basically said ‘what the hell is this peremptory interrogatory? How is it consistent with ACNP bylaws? If someone is griping to you about us let him bring forward an action through the standard ethics committee process. Otherwise, go take a bath.’

Soon afterwards, I received a phone call from Paul Jacobs who said ‘Barney, I need to ask you about what has happened at ACNP’. Up to this point, Paul was aware that we were under an ethics investigation, but because of the instructions from the College I was not free to discuss with him how that was going or what the outcome was. So Paul calls me up sometime in late May of 2006 and says ‘I need to know what's going on with the college’. I said ‘Paul, I've told you before I really can't tell you’. He said ‘Well I've just received a letter from a gentleman called Robert Hawk, who is the attorney for Corcept Therapeutics’. ‘Oh’. ‘And Robert Hawk has informed me that ACNP told him

that you and Bob Rubin were admonished by council for displaying your poster in 2004.'

I said immediately 'Paul, thank you very much. You've just made my day'. Because I realised someone at ACNP had leaked this confidential information to Schatzberg's attorney. ACNP had therefore broken confidentiality, while concealing the fact from us and, as we later wrote to council, this released us from any obligation to hold confidential the events from our point of view. Basically Robert Hawk, acting for Schatzberg, was attempting to smear us with this information about a sanction, and through that mechanism to dissuade Paul Jacobs from going ahead with publishing his critical piece. In other words they were trying to shut down criticism of the company and of the company's claims, and the means of doing that was to smear us. The confidential information that enabled them to attempt that came from ACNP itself. Paul Jacobs sent us a copy of the letter from Hawk, which confirmed our suspicions. Mr. Hawk also stated in his letter that Bob Rubin and I "have made numerous false and malicious statements regarding research related to Corcept's product..." and that the sanction by ACNP "bears on the probity of Dr. Rubin and Dr. Carroll."

Bob and I really took ACNP to task in several written communications for this violation of confidentiality. It was a low day for ACNP. The president at the time was Kenneth Davis. No officer of the College has had the integrity even to acknowledge what they did, much less to apologize to us. We later learned that they had acted out of fear, because Schatzberg or his company were threatening to sue the College. So they threw us under the bus, as the saying goes.

Then in late 2006, a second ACNP ethics complaint was filed against us. The usual medieval inquisitional process – we were never shown the original complaint, we were never informed who was the complainant. Can you imagine this in the 21<sup>st</sup> century? The notice of complaint sent to us was written by the incompetent ACNP attorney. It was a careless farrago of smears, nonsequiturs, and specious objections to our scientific critique of the new 2006 Schatzberg publication. Here is a sample: "...you engaged in non-collegial behaviour by, among other things, calling the findings of the authors 'invalid'..." This was in reference to our letter to editor of NPP critiquing Schatzberg's 2006 publication. We assumed the complainant was Schatzberg. In later correspondence, the ACNP secretary, Alan Frazer, revealed that it wasn't Schatzberg. If it wasn't Schatzberg personally then it had to be Belanoff acting as Schatzberg's proxy, because it contained information that Belanoff could not have known without Schatzberg's participation. I should explain that Belanoff is Corcept's CEO and a co-founder of the company with Schatzberg. We don't know why Schatzberg would want to use Belanoff as a stalking horse – Belanoff is not even a member of ACNP. So that says something about Schatzberg's style. Basically, the new charges were another laundry list of specious complaints about us, which we rebutted very effectively. Another element in this second round of ethics complaints against us was that we began to suspect the Chair of the Ethics Committee, David Braff, was not acting impartially.

We had earlier sent Braff the document that I called the Corcept Timeline, a document that you have, along with the message that this contains sufficient information for the ethics committee to move against Schatzberg. Braff's response was to deep six it. So that was our first indication that he was acting in a manner that was not impartial. The second indication we had was that the charges he relayed to us in November 2006 were so manifestly contrived and specious that he should have known they were non-substantive and he should never have proceeded with this second ethics inquiry. But we believe he acted in bad faith, which in itself constituted another harassment of us.

The third indication was we got a back channel message that Braff was having frequent telephone conversations with Belanoff around the time of the ethics committee deliberation, and that he acted with bias during those deliberations. Whereas our approach was you don't try to tamper with the jury, and we studiously refrained from any contact with any member of the ethics committee throughout this entire process. We sent ACNP council a formal complaint about Braff, but they hid behind the ACNP attorney and refused to act against Braff for malfeasance.

The final resolution of the second ethics complaint was that none of the charges was upheld. The way that was communicated to us was in weasel words - they could not bring themselves to say the charges were thrown out for lack of substance, so, paraphrasing, they expressed it as 'the committee was not able for the lack of evidence to substantiate the charges made against you so therefore they are dismissed.'

I wrote back to Alan Frazer the ACNP secretary, I said in effect 'Alan this is not acceptable. This was a bunch of phoney trumped up charges in the first place, and you should be ashamed to send me a letter like this in an attempt to close out the matter.'

So you can gather through all of that that our warm feelings for ACNP are not what they used to be back in the '70s and '80s. I think part of the problem is the ethic in the society has changed. And it changed because the leaders of societies like ACNP, just as the leaders of academic institutions and medical schools, have failed to rein in the outliers, people like Nemeroff and Schatzberg, and Biederman and Keller. These outliers came to be seen as role models and in many cases came to hijack control of the organizations. It has been a sad decline, I think, for the entire field. Now, with new regulations being discussed, the entire field will pay a price in increased bureaucratic burden because the leaders of academic medicine failed to do their jobs of guarding the ethics and standards of their organizations.

The final insult to us was in March 2007, after our complaint about Braff was denied, and after we raised a new issue to do with a publication by Nemeroff in Neuropsychopharmacology. This was the infamous November 2006 Rapaport-Keller-Nemeroff study of Janssen's drug risperidone in refractory depression. We made a prima facie case that the report appeared to be fraudulent, and it was later retracted under our pressure. Nemeroff was a co-

author of that publication in his own journal - just one more example of the self-dealing that the New York Times called 'incestuous.' The article came out in late 2006, and we made an issue of it in early 2007. In March 2007 we got a letter from the president William Carpenter basically saying we think you two guys should resign from membership of ACNP. Carpenter's letter was essentially a litany of whining on behalf of council. Bob and I wrote back and said in effect go jump in the lake – we are waiting for the leadership of ACNP to show some spine.

**That's an extraordinary fall from grace for ACNP isn't it?**

They are not the group they once were. But, you know, they are not the only professional organisation to go through such a decline. Look at the American Medical Association. It used to be, say in the '50s, the premier organisation in the country. Nowadays I think they are lucky if 25% of physicians have membership. And they are increasingly seen as irrelevant dinosaurs when it comes to issues like national reform of health care. I think ACNP is going in a similar direction. They've lost their original spirit and ethic, and they've become corrupted, by cronyism and money.

**In terms of some of the players in all of this, there is a real feeling at times that there is bullying involved and corner street tactics. Does that seem a reasonable way to sum it up?**

Several people tell me that Nemeroff is a person they dare not cross because he will retaliate. They point to instances where they know he did retaliate. I call Nemeroff the Tom Delay of psychiatry. He has also been described in Mafia terms as 'Boss of Bosses.' He's an operator; he has inveigled himself into positions of trust in many organisations, including NIMH. He's very capable and willing to exert a malignant influence behind the scenes with grant applications, with job opportunities, with recommending people for fellowships or faculty appointments, with giving the nod as opposed to not giving the nod for investigators to participate in corporate funded clinical trials. If Nemeroff is consulting for, lets say Glaxo, and if he doesn't like Dr X in some city, people tell me he's quite capable of turning off that site and denying business to Dr X. I just can't tell you how many people have related their fear of him to me. He does not hesitate to badmouth those who cross him. The list of casualties in his malignant wake is very long indeed. Schatzberg also has shown himself to be quite capable of smearing, ad hominem, mean spirited attacks on critics. Most recently he did that to Allen Frances over the controversy surrounding DSM-V. And, as you can judge from this interview, Schatzberg will stoop to intimidation through his attorney.

**Barney, how much did Bob and you put the conflict of interest issue on the map? Or put it the other way - who else do you think contributed to raising the profile of this issue?**

Look at it this way. Who is the poster boy for conflict of interest issues? Nemeroff. Who was responsible for outing Nemeroff in two international incidents? Rubin and Carroll. There's your answer.

**Well if you led the charge, are there people you could pick out that have also helped raise the issues? This whole area has become an area of**

**great debate and is it just down to the work that you and Bob did or have there been more tributaries to this river?**

Let me answer you in a couple of ways. At the level of individual scientists there is an expression that Bob likes to use, which is 'chocolate soldiers'. There are a lot of people who will become indignant about what they see happening but they won't stick their necks out. And we have encountered that repeatedly. We would flush out an issue and expose Nemeroff. We would get all sorts of complimentary e-mails from folks who were still firmly within their own foxholes and never poked their heads out. So, in terms of Nemeroff, I would say but for Bob and me it would never have happened.

Then there is another group of people who speak out against conflicts of interest but they are for the most part not working scientists. Some of them are physicians like Marcia Angell or journalists like Alison Bass, who have been public about it. Certain bloggers like Aubrey Blumsohn in Britain have been very vocal about it. Or Philip Dawdy who runs the Furious Seasons website. Or Margaret Soltan who runs the University Diaries blog – she is a professor of English. Or Daniel Carlat, who is not a working scientist though he is a very astute and well informed clinician-educator. I should also mention Roy Poses at the Health Care Renewal weblog, and Howard Brody. But frankly, among the ranks of working scientists there are very few who dare speak out. And then you've got the professional organisations like the Institute of Medicine and the Macy Foundation, who in their institutional way come out with recommendations for systemic change. Their voices are helpful as well. But what appears in their publications is like the second derivative of the stuff Bob and I are doing. The element of scandal and the whiff of corruption are sanitised out of their documents. Bob and I like to say we are not professional ethicists but we know corruption when we see it.

**The kind of conflict of interest that you are talking about here is really an insider trader type of conflict of interest. Does that seem right to you?**

Much of it is yes. Much of it is an issue of role confusion. People like Zach Stowe, Charles Nemeroff, Alan Schatzberg and Martin Keller behave as though they are part of the marketing arm of corporations. They fail to respect the boundary between their academic ego and their corporate consulting ego. So you look at what they actually do and you scratch your head sometimes and wonder when they find time to fulfil their primary academic missions. If you look at the material that Senator Grassley released, for instance, on Nemeroff's speaking schedule for Glaxo, he was on the road an inordinate amount of time, and that was just for one company. He opens himself up to charges of conflict of commitment, especially when he is being paid salary from NIH sources, and it is clear he lost the ability to control his behaviour in the face of perverse incentives.

**The latest person to be called on links to Pharma is of course Zach Stowe.**

I'm rather sad about it because he was a resident at Duke whom I counselled about his academic goals, and it seems he has been led off the path by Nemeroff.



**There's the aspect to all this where people like Stowe or Nemeroff have minimised the risks linked to the treatment but there's also the aspect here in the States, where even in the case of giving drugs to pregnant women or antipsychotics to infants doctors, academics and even people themselves seem to feel the need to treat. What is it about the US style of thinking that leads them down that path? It isn't just that experts are being paid by industry give this message, the audience are clearly open to this kind of message.**

The reason has a lot to do with managed care. In that world, it is important that you demonstrate that you're doing something. When managed care first came in, the insurance companies would call daily, and if we had an inpatient in the hospital, say, they would call on the 2<sup>nd</sup> day and demand to know what drug the patient had been put on for the diagnosis of depression that we'd given the patient. We would explain that we were still assessing the overall diagnostic picture and the overall needs of the patient, and that we hadn't made a decision yet. So they would deny coverage for that day.

That mind set over the period of the early to late nineties was drilled into the profession in America. These were translated almost into quality standards. If you make a diagnosis of depression, why haven't you prescribed an antidepressant drug? If you make a diagnosis of psychotic depression, why haven't you prescribed an antipsychotic drug immediately? Those external constraints on practice that managed care brought have had some far reaching effects.

Now, there's also something to do with the American character. There's the old medical joke about the difference between the surgeon and the physician. The surgeon walks up to a resident who's pondering about a patient and the surgeon demands 'don't just stand there, do something'. And the physician walks up to the same patient and says 'don't just do something, stand there'. Meaning sort it out rather than reflexively do something that is going to make you feel better but may complicate the clinical problem. I'm afraid that it's just in the American character that there are more surgeon types than physician types, even in psychiatry.

**How successful will these guys who are the hired guns for the pharmaceutical industry be at being able to turn the issues round and portray it as a media witch hunt?**

They are already trying to do that. There is a conference due to take place in Monaco in November. This is one of these groups created by Pharma - The International Forum for Mood and Anxiety Disorders. They will be gathering in Monaco and one of the topics featured, I quote to you, is '*Making sense of media attacks on experts. Is this a wanton witch hunt?*' So you know they are already trying to portray these exposés as a witch hunt. This point of view has some very vocal supporters, like Thomas Stossel at Harvard, who frequently writes Op-Ed pieces along this line.

Recently they even got some support from the editor of Nature Medicine. In the June 2009 issue of that journal there is an editorial that basically says 'lets all hold hands, lets agree to dial down the heat, lets just focus on outright

fraud and not get excited about anything that falls short of that'. More or less the Rodney King plea 'can't we all get along?' My response to that is that the dangers of competing financial interests go well beyond just outright fraud. What you have is a pattern of relationships that indicate a loss of professional integrity.

Another source that I often call on in this regard is the Canadian sociologist Jane Jacobs. I don't know whether you are familiar with her? She's written extensively on professional roles vs. commercial roles and about the need for a bright line between those two.

Back in the '60s, '70s, '80s many academics would freely and gladly consult with pharma, giving them advice. I certainly did, and I used to joke that my main role as a consultant to pharma was to prevent them from wasting their money on fads. I spent a lot of time talking them out of projects rather than cheerleading for projects that they had underway or were planning. I certainly never was a spokesperson for them in the way that you see nowadays. I can show you things now in my file of press releases from various corporations where academic key opinion leaders are trotted out to endorse the product or endorse the new discovery, clearly part of the marketing effort of the company rather than a genuine academic opinion, in a way that would have been inconceivable in my day. It would have been unthinkable to shill for Lilly or Glaxo or Corcept on a press release. But nowadays it happens all the time.

**Can I ask you, in the last 8 or 9 months or so we've seen people who were senior figures in leading universities having to resign in a way that has been pretty well unprecedented, do you think we've reached a turning point or do you see any real change happening? Do you think for instance that the structural forces that have brought us to this point are still in place and until they are changed that really the field will continue to throw up further Charlie Nemeroff, Alan Schatzberg type figures?**

Time will tell. One very positive development is that medical schools now are revising their policies to prevent faculty members from giving promotional talks for pharmaceutical and device corporations. The latest announcement of this kind came from Emory itself. As that posture spreads, the worst of the abuses will be contained. On the other hand, human nature being what it is, a Charlie Nemeroff or a Zach Stowe or an Alan Schatzberg will find ways to get around the regulations, and I predict that one effect of these new medical school policies will be to rack up the money laundering through medical education communications companies. The CME type events will be now emphasised, and the same cast of characters will have a fig leaf to continue to do what they do today, which is to shill. So it's going to take some watching.

**Why do you think the field as a whole has been so prepared to let some of the senior figures say things that we all know they can't really believe – why do we let them shill? Is it because we are also being brought to the major meetings by the pharmaceutical companies these days? We're all on the gravy train in one way or the other?**

I think that's part of it. But part of it, frankly, is just a general degrading of professional standards. Students go into medicine nowadays with the objective of getting rich. In my day nobody went into medicine with the objective of getting rich. They expected a comfortable professional life. They were not out to become millionaires. That was unthinkable. But now you have medical students going to medical school with that in mind, selecting the most highly paid specialties, and basically turning their profession into a business. Translate that to the academic setting and you get the Nemeroffs and Schatzbergs, who will bend and finesse the rules any way they can for their own purpose.

**If the driving force behind this is the logic of the market place, that we are in one sense or another all in business, it's very hard to see how that's going to be reversed. How we are going get back to people being happy to accept being professionals?**

This is a trend that has been at work for decades. I can remember at Duke in meetings of the clinical chairs in the 1980s, the least respected department in the medical school was paediatrics, because it didn't make money. It was a real eye opener to see the contempt expressed towards paediatrics by the Departments of Surgery and Medicine. So, that mindset goes back a long way. And it is throughout the profession of medicine, it's not just in psychiatry.

That is one reason for the difficulty in recruiting primary care physicians, and rural physicians and paediatricians in a country like the United States. I just listened to Obama's speech on health care reform this morning and, you know, here we are spending I think 50% more per capita than other countries and getting less for it, while droves of trained physicians are going into occupations like plastic surgery and interventional radiology and so on.

**Bob Rubin has been a key player in all this. What's his background?**

Bob and I are two of the pioneers of psycho-endocrinology. We first met up in 1968 in Melbourne Australia, where I was still in training and Bob was visiting for a WPA conference. I was assigned the role of local host to him for the three or four days that he was in town. And that turned out to be the start of a life long friendship. He was at that time at UCLA. And when I visited the APA meeting in San Francisco in 1970 I made sure to go by UCLA and visit with him. He wanted me to come and work there, and he introduced me to his chairman, Louis Jolyon West - Jolly West. Jolly was affable but nothing tangible happened. So I went along and met with some other people and when I did finally come to the States in '71 I ended up in Philadelphia. By that time Bob had moved to Hershey, Pennsylvania, which was 60 miles from Philadelphia. So he and I were meeting each other again very quickly. After a year or two he left Hershey and went back to Los Angeles, and so we had a long distance relationship from that point on. But we always made a point of catching up with each other at APA and Biological Psychiatry meetings.

In an article that he wrote with Arnold Mandell in 1966, Bob was the original articulator of what is now called the Neuroendocrine Research Strategy for depression. This basically says what you see coming out through the hypothalamus-pituitary-adrenal axis is a reflection of what's going on in the

limbic system. Neurotransmitters that drive those neuroendocrine changes may be disturbed just as neurotransmitters that drive mood circuitry may be disturbed. Bob really was the first person to clearly articulate that.

Bob has had a very distinguished career, with continuous NIMH funding for gosh 30 years or something. He had a very productive laboratory at Harbor Hospital at Los Angeles, then went to Pittsburgh in 88 or thereabouts and stayed 16 years running a neuroscience research program at Allegheny Hospital. He came back to Los Angeles in 2004 as Chief of Psychiatry for the VA system in Los Angeles and Vice Chairman of the Department at UCLA, and that's where he is now.

### **What's his motivation for getting stuck into these conflict of interest issues?**

Same as mine. Somebody has to call out the rule breakers. Both of us view this, I think, in sociobiologic terms rather than moralistic terms. If you look at the evolutionary psychology of ethical codes, they are the glue that holds societies together. Within any society you get what John Maynard Smith called a stable balance between co-operators and defectors. Part of the dynamic within societies which have ethical codes is that defectors have to be called out or punished for their defections, because if they are allowed to run rampant then the society as a whole ceases to function. The original theories of this Evolutionarily Stable Strategy – ESS as Maynard Smith called it – were applied to the case of Hawks and Doves, but it also applies to co-operators and defectors. The original ideas, coming from game theory, were that there was simple reciprocity or tit for tat gaming strategies, interpersonal interaction strategies over time that would rein in defectors. Then we have the concept of indirect reciprocity, originating with Robert Trivers and William Hamilton, where reputation became a very important variable in the dynamic. More recently we have the formulations from Fehr's group in Switzerland, moving from indirect reciprocity to so called strong reciprocity, which involves a term that he calls altruistic punishment.

Altruistic punishment means the person who calls out the defectors pays a price for doing that. Between the two of us, Bob and I have incurred about \$20,000 in legal fees defending ourselves against Schatzberg. That is one very tangible example of the cost, to say nothing about the several years of harassment and, in many places I am sure, some suffering of our reputations with people who have heard one side of the story but not our side. Why do Bob and I do it? I guess because we can't help it. It's a pre-programmed or hard wired response to the shenanigans that we observe. But it does set us apart from the individuals whom Bob calls 'chocolate soldiers,' who get indignant about what they see, but who do nothing about it.