

15 Rachel Gittelman Klein

Children and psychopharmacology

Could we begin, Rachel, with where you were born?

I was born in Paris, France, and lived there until I was 15, when my family emigrated to the USA. My father and mother, who were Russian born, decided to leave France immediately after the war in 1945, because they had experienced great hardship during the war and the common wisdom then was that there would be a world war between the Soviet Union and the USA and that western Europe would be squeezed between the two. However, because of the McCarran Act, which imposed quotas on immigration based on country of birth, it took 4 years for them to obtain visas to emigrate to the USA.

So you had to move schools and learn a whole new language. How did you cope with all that?

I worked extremely hard until I became fluent in English. I went to Midwood High School in Brooklyn for 2 years, and after graduation went to City College in New York City. I worked for a few years and then enrolled for a PhD in clinical psychology.

Why did you go into clinical psychology? How did the field look then to you? What was your interest? What was your motivation?

My motivation was to work with children – with normal children. During college I had a job as a group worker in an after-school programme in a community centre located in a New York ghetto. I had been resoundingly successful. The kids loved me, I loved them. I was determined to show them that there was a world outside the ghetto. We did all sorts of things together in the city. It was really terrific. I thought I would continue doing that sort of work, but on a higher level, and I needed a degree. Also, at the age of 18, I married someone who became a psychologist and that also influenced me.

So your PhD thesis was on...?

My PhD thesis was on the prognosis of schizophrenia. It seems inconsistent with my original goals, but many events occurred that altered my trajectory. Firstly, I decided to work towards a degree in clinical psychology rather than developmental psychology. At the time, clinical training was the most prestigious.

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Secondly, probably the key event in my life, one that was to play a major role in my professional life, I got a job for the summer at what was then Hillside Hospital, where Max Pollack, Max Fink and Don Klein were conducting some of the first systematic psychopharmacology research. Getting the job was pure serendipity. I met Max Pollack at a resort, we became friendly and he offered me a job to evaluate patients in their ongoing studies. I was a graduate student in clinical psychology and the whole idea of using medications in psychiatric patients seemed rather distasteful.

Can you get hold of that for me?

I wasn't as passionate against medication as many people then were. But I did feel that, if it worked, it did so only during active treatment and that there had to be treatments with greater promise. I viewed medication as a temporizing treatment strategy, and therefore devalued it. At the same time, I was extremely critical of my training. Even though I had chosen to study clinical psychology, I was appalled by the content of my graduate training. You see, I had not studied psychology as an undergraduate student. I had studied literature, and assumed that clinical practice was rooted in empirical data. I was amazed at how little was known, and at the fact that we were being taught all these dicta without any basis in fact. I felt that clinical psychology practices were really questionable, and that the same was probably true of psychopharmacology.

Through my experience at Hillside with the research team, I developed immense respect for the people conducting the trials. They were intelligent, serious, caring and weren't out to prove an ideology. They were trying to get patients better, and to understand the therapeutic process. You have no idea how refreshing and exciting that was. My job was to evaluate patients at the initiation and the end of a 6-week study that compared Thorazine, imipramine and placebo. Thorazine was already on the market, but imipramine was not. I saw patients whom I will never forget, patients with retarded or agitated depressions, people I wanted to run from because they were in such pain and caused me such pain. Yet they walked into my office 6 weeks later – I get chills even now thinking about them – and they were well. They were talking with me the way you and I are talking now. You couldn't dismiss that sort of event. It was very very dramatic.

At that point I thought that the objections – obviously there were problems – did not vitiate the benefits that one saw in 6 weeks. This experience, combined with a lack of respect for other unfounded therapeutic practices for which wild claims were made, tilted me towards the direction of empirical approaches to treatment.

Did this begin to put you at odds with the other people training with you?

In a way I had joined the enemy. But I never saw it this way. I never was trying to prove anything and I ignored others' opinion. To this day, I've never been invited to give a talk at Columbia University Teachers' College my graduate school. There's still a great deal of territorial distance between those who do

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study with schizophrenic and autistic children. He himself had an autistic child. I think that's why he became interested in doing work with these youngsters. At the time, there were very few people who even knew how to conceptualize a psychopharmacology study. He hired me to assist in preparing a grant submission and run the study. We compared Thorazine to Benadryl (a compound that was not expected to have clinical efficacy, but would have similar side-effects to Thorazine) and placebo in very young children with autism and other severe developmental disorders, what we now call pervasive developmental disorders. This work was never published, by the way, which is too bad. We found that Thorazine was markedly superior to placebo and to Benadryl in reducing disruptive, hyperactive and uncontrollable behaviour.

At that point, with all of those conditions, there was this big hostility about it being caused by the parents - the schizophrenogenic mother or the cold kind of family that causes autism. Did you run into problems then, trying to treat this kind of condition with pills?

Well, I never thought we were treating autism. I thought that perhaps we could make the children more manageable and the family could avoid institutionalizing the child. These were not trivial goals, since many autistic children ended up in chronic residential settings, and preventing institutional care would be a major step forward.

I never bought into the schizophrenogenic mother. I never was tempted by Freud. Perhaps it's because of my own personal background, although in retrospect you can explain anything, but I felt there was no way parents could be so powerful that they could possibly cause such devastation in a human being, since there were so many other influences in a child's development. Essentially, I believed that development could be perturbed, but not completely reversed, except perhaps with severe malnutrition or other brain-damaging events, but not by subtle interactional processes.

Moreover, I felt that blaming parents was extremely destructive and was quite hostile to this theory of infantile autism, in view of the total lack of evidence for it. The parents were desperate. They had the least resistance to using medication since they were grasping at anything that could possibly help their child. The use of medication was not a major issue for the parents, though it was for the field.

Was this the point at which you began to focus more clearly on childhood disorders or did you go back to adults at any point?

Yes, I think that experience pushed me into the child area. Essentially, we do what we know how to do, and I'd become quite expert at assessing children and interviewing parents. At that point, Don Klein was developing a project with children who had separation anxiety. He needed someone who could develop the protocol, run the study, etc., and I guess I had become a rather rare commodity. I was hired to do the study at Hillside. I had originally left Hillside for Downstate because Don and I had developed a personal relationship that had become rocky. By the time I returned to Hillside to conduct the study with

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effort to treat the child without medication and, if we failed, there would be the option of medication. No doubt, there were some who refused, and others who would not even consider the possibility of medication and were never referred. But most of those who accepted the use of medication did so because we were so sincere in our attempt to help them, before we suggested that perhaps it was time to try medication. By the time we did so, we had usually developed an alliance with the families, who were confident that our effort to help the child and the family was genuine.

When you talk about looking at the outcomes, this was really in an era before rating scales had begun to be used widely, before they'd become the sine qua non that they now are. What kind of outcome measures were you looking at - people being able to get back to school? Real-life outcome measures?

The Rutter scales had been published, and we used them. In addition, we made up our own rating scales. I had experience with the systematic assessment of adult patients, for whom there were already quite a few scales. These weren't necessarily all that satisfactory, but at least there were established methodologies to assess symptomatology, clinical progress and improvement. We followed the model of generating measures that reflected the particular psychopathology under study. By the time we started the study, we knew these children pretty well and had a good sense of what they were like.

That this must have been true is, in a way, documented by the fact that the DSM III diagnosis of separation anxiety, which I essentially wrote, was based on those study children, and it is one of the childhood disorders that has been subjected to least modification over the ensuing two versions of the DSM. It has remained virtually unchanged over 16 years.

And imipramine helped?

It helped enormously. In fact, I felt that the statistical results did not do justice to the clinical impact of the medication. It transformed the children. By the way, the very first child we treated with imipramine was my own 4-year-old daughter who had severe separation anxiety. She responded marvellously. That's not the reason why I studied those kids, but that's probably why I understood them so well and was comfortable doing the study, although I must tell you I was extremely nervous when I gave my child her first pill. But this was a 4-year-old little girl who could not get out of bed in the morning unless I went into her room; who could not go to sleep at night, who could not be in a room by herself in her own apartment. There was this darling little girl who could no longer function and enjoy life, and who would literally panic if I stepped away from her. But she did not have panic attacks *per se*. She was fine if I was with her and never panicked spontaneously. After her being on imipramine, she would play by herself in her room in the morning. It was truly uncanny - could it just have been coincidence? Perhaps, but I was encouraged by that experience, all the more so that she did not know she was taking medication. It's of some interest that she's now a thriving young woman who shows no sign of anxiety.

So the disorder is not invariably a life sentence. I thought our study results were phenomenal, and that the tests of significance did not reflect the quality of change. But one study doesn't make a finding. We wanted somebody else to do the study again, but nobody did.

Why not?

I don't know. There were little studies that yielded inconclusive results. These clinical treatment studies are not easy to do. It's very hard to recruit cases, it's expensive, you need trained staff. I kept puzzling about the same question: why doesn't anybody try it? They shouldn't believe only one study. So we decided we would have to do it.

Many years later we got a minimal grant to repeat the study, but this time the children didn't have to have school phobia as part of the separation anxiety disorder. Unfortunately, we were able to recruit only twenty children and the study was negative. We obtained no imipramine-placebo difference, and I must say the statistical results reflected reality this time. I was very unimpressed. As impressed as I had been the first time, I was completely unimpressed the second time. I understand that there's a new study that finds significant efficacy for imipramine in children with separation anxiety. However, I have not seen the data. Maybe that's the reality of clinical research – results are not positive in every instance, even if one is dealing with effective compounds.

So, could it have had to do with the fact that the first trial you did was looking at a more severely ill group of people and...?

It may be that children in our first study were more severely ill, that the practice of child psychiatry had changed so much in the interval between the two studies, that different patients with separation anxiety were referred for treatment, and that these differences were not obvious from a mere clinical exam.

When you say things have changed so much in child psychiatry, what had changed? What was changing? What was happening?

I think that by the time we conducted our second study, many more child psychiatrists were using medications and perhaps children treated successfully in the community were not referred to us. No child in our first study had received medication, except for a few who had been given Compazine by paediatricians because of complaints of stomach aches and nausea when separation was attempted, such as when they tried to go to school. By the time we did the second study, I think our work and others' work had become quite popular, and medication was much more commonly used in anxious children. In addition, there were many more child psychiatrists, so that treatment availability had greatly increased. These factors may have affected the clinical populations we studied at the two time periods.

Were there any key people in the field whose work or public attitude helped to change things? People like Leon Eisenberg, for instance.

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Early on, Leon Eisenberg was critical. He was one of the very first to conduct psychopharmacological studies in children with behaviour disorders, although my impression is that the work had very little impact on clinical practice. In addition, the Montreal group with John Werry and Gabrielle Weiss published the most systematic trials of stimulant and phenothiazine treatment of hyperactive children.

It's difficult to pinpoint any one person as being key or having a major influence. I think, perhaps, the greatest influence was the meteoric change that was taking place in adult psychiatry. As hard as people tried, they could not escape the tremendous progress and the ensuing payoff. Adult psychiatry really had more influence on child psychiatry than the few child psychiatrists who were doing unusual things. A case in point is our imipramine study of separation anxiety, which emanated from adult psychopharmacology. This work did not only have treatment implications, it also represented a major diagnostic shift. For the first time, a childhood anxiety state was singled out as deserving specific attention, and as having specific distinguishing pathological features. This approach was very unusual in child psychiatry, where descriptive diagnosis in general was not a hot topic, much less diagnostic refinements within the anxiety disorders. This work led to the inclusion of the disorder in the DSM-III and has withstood the test of time -as least thus far. These developments were entirely initiated by the clinical observations made in adult patients by Don.

The study of separation anxious children had further scientific ramifications. Since we had gained experience in studying medication in children, our interest widened. We eventually conducted large treatment pharmacotherapy studies of children with attention deficit hyperactivity disorder (ADHD), and have gone on to do similar studies in children and adolescents with other disorders such as major depression and conduct disorders. Directly and indirectly, child psychiatry has been altered from without, by adult psychiatry, rather than from within. Of course, and fortunately, that has changed, but not as much as one would wish.

What you say may help to explain why things didn't change in the same way in the UK, in that adult psychiatry didn't change the same way as it changed in the USA. We didn't have this big watershed around 1980 where things changed from one mode of being to a completely different one. It's been much more consistent throughout, which has left UK child psychiatrists uninfluenced by a change happening in adult psychiatry.

I think the other change that took place in the USA, which also distinguishes it from Great Britain, is the shift to DSM-III, and the great influence that the latter had. In contrast, I think the DSM-III was resisted and viewed with hostility in Great Britain.

Yes, it was seen as one of these other things that we get from the USA that we are going to resist if at all possible. Something like that.

Something like that. In the USA, diagnosis became important, just as it had become important in adult psychiatry. And it also influenced practice in terms of leaning towards psychopharmacology.

You say you were asked to write the criteria for DSM-III for separation anxiety. Who asked you or what does it mean to have to write criteria? Is this the kind of thing that gets seen from the outside as the behind-the-curtains manoeuvring? How above board was this?

It was very above board. A committee on childhood disorders was put together by Robert Spitzer, who was in charge of the DSM-III. Initially, it consisted of a small group whose members had conducted systematic clinical research in child psychiatry. The key was to avoid unsubstantiated aetiological theory and to develop specific inclusion and exclusion criteria. As the process became increasingly more political within the American Psychiatric Association, working groups were enlarged to meet various constituencies. You understand, there was tremendous hostility towards the DSM in a large part of the psychiatric community convinced of the importance of 'dynamic' rather than descriptive diagnosis.

We were each assigned different jobs. Because of my clinical experience with children with separation anxiety, I suggested that the disorder, which did not exist in the nomenclature, be included. I offered to write the text describing the condition. It was reviewed by the committee, questions were raised, suggestions were made. The criteria came later. That was a much more collaborative process.

I don't recall how decisions were made regarding how many inclusion and exclusion criteria there should be. Those issues, though arbitrary since we had little to guide us except our clinical experience, followed general principles. For example, there should be enough opportunity to diagnose individuals with a specific disorder but somewhat varying clinical presentations. We knew, of course, that reliability was likely to be improved if relatively more criteria were included. Consequently, whenever possible, we avoided having very skimpy criteria sets. Also, we tried as best we could to make sure that diagnoses had high enough thresholds to avoid having high rates of false positives; at the same time, the diagnostic threshold could not be set so high that false negatives would be common. Back in the 1970s, when DSM-III was formulated, for the most part, we had only our clinical fund of knowledge to rely on. It's remarkable how well we did in many instances – not all, of course. I'm not sure things are much better now.

By this time, you had also begun to move into the ADHD field. Can you tell me when you began to do that and how the field looked at that point in time?

By the time I went back to Hillside to work with the separation anxious children, the work by Eisenberg and Keith Conners on the efficacy of stimulant treatment in hyperactive children had been published, but there was very little else. I thought the findings were extremely curious, and took them with a grain of salt. I'm not an easy believer; I don't join the bandwagon very easily – that's probably why I went into research. Don and I discussed it and he also found it very interesting and curious. We started treating a few children clinically and were impressed. But we didn't quite buy it, so we went on to design a controlled study.

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Why not? Was it a problem that you would give this drug that was a stimulant to kids who were overstimulated to begin with?

Exactly! And how could one make sense of this? Traditionally, what had been done in child psychopharmacology was a straightforward translation from adults to children. Even the work I did with the pervasive developmental disorders extended the use of Thorazine in adult schizophrenia to children, the reasoning being that these children had something like schizophrenia. Although I didn't believe that this was the case, it was conceivable that Thorazine would be helpful. Child psychopharmacology essentially consisted of transposing practice down to younger individuals rather than positing new ways of looking at children.

Don was the first one to propose a different approach to the treatment of a childhood disorder, in that the use of imipramine in the separation anxious children derived from a specific theoretical model of child psychopathology. He posited a relationship between separation anxiety in children and adult panic disorder that led to the drug study in children. With the hyperactive children, the observation of stimulant efficacy was completely accidental, just as the rest of psychopharmacology, but it had been so long since the early reports by Bradley, which I'd read and did not find all that compelling.

This goes back to 1936. Did you ever meet the man?

No. I didn't know him at all.

The other person who was doing work with children who may have been using methylphenidate was Laretta Bender. Did you have any contact with her at the time?

I met her, but never knew her. Barbara Fish, her student, conducted controlled psychopharmacology trials with schizophrenic children or various sorts of developmentally impaired children. I certainly was familiar with Barbara Fish's work, but was most impressed with the work of John Werry, Keith Conners and Leon Eisenberg. However, I had to see for myself. In a way, we started doing that work out of disbelief. In fact, that's why there is so much research on the treatment of children with ADHD – hyperactive children. Many psychologists have found the notion that medication is effective distasteful and have gone into the field with the expectation that they will be able to disprove the drug effect or improve on it. Every time they have tried, they have failed. We were not trying to find fault with the treatment, but were sufficiently intrigued to see for ourselves.

At that point, during the 1960s, how did the disorder look? What did people think it was? There are a whole load of theories about it, for example that it was food allergy syndrome. How did it seem during the 1960s? Was this the minimal brain dysfunction period?

Yes. There was the minimal brain dysfunction view of Paul Wender and others, which was held by the more 'organically' minded, but it was a vague concept that explained, perhaps, too much. There was also the family theory that argued that parents had failed in the socialization of the child. Those were two major

trends, but there were also other family theories that posited that the child expressed the family's pathology, the systems view of the family that also explains everything. The most influential academic theory was the learning theory of maladaptive behaviour, which advocated that, somehow, the child's experience had been such that he had received positive reinforcement for negative rather than appropriate behaviour. It was expected that this could be rectified through behaviour therapy that was designed to reward the child for behaving appropriately, and to provide negative consequences for misbehaviours.

The drug studies we did were atheoretical. We weren't making any assumptions about the nature of the antecedents. We never assumed that medication efficacy proved that a disorder had a strictly biological origin. You could treat so-called psychological reactions with medication, and you could treat biological phenomena with environmental manipulation. Aetiology was not troublesome to us in terms of justifying the treatment.

This was the mid to late 1960s when you began to treat the first few children. The whole field then begins to take off to some extent and you get things like food allergy syndromes beginning to come into play. How did you see it going? Who were the key players? Why did things go the way they went?

You raised the issue of resistance, consumer resistance or professional resistance to using medication; that attitude was most influential in the treatment of hyperactive children. It had been relatively easier to offer medication to parents of children with separation anxiety or autism or schizophrenia. But here we encountered enormous social opprobrium. Partly, in the USA, the issue had racial as well as political overtones. Many of the children being treated for hyperactivity were from ethnic groups. It was argued that medication was a form of pharmacological genocide, by interfering with children's free will and controlling their behaviour. That this was the case, it was argued, was documented by the view that the behaviours of hyperactive children could be interpreted as resisting the irrational demands of an authoritarian world. Essentially, these lively, rambunctious children were being turned into passive pawns. These views, I should say, were not limited to minority children, but to all hyperactive children. The diagnosis was challenged as representing teachers' inability to tolerate children's expansive, enthusiastic style.

Who was actually saying this kind of thing and when did it reach Church of Scientology level? For the first few years, it had to have been okay, but when did it become a public issue?

Thomas Szasz, a psychiatrist, was a major figure in the antipsychiatry movement. By the early 1970s, treatment was very politicized. (The Church of Scientology came on the scene a little later.) Remember that this was pre-DSM-III, there were no diagnostic criteria, or objective quantitative measures. There were not yet scale standards for quantifying hyperactivity. We faced the dilemma of how to diagnose ADHD. Initially, strong resistance came from the psychiatric profession and other care providers. There was immense hostility to

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the notion of giving medication to hyperactive children. In addition, the few who used stimulants justified it on the basis that they used them only in children whose hyperactive behaviour had an 'organic' cause, and not if the disorder was 'emotionally' based. Therefore, some claimed a need for neurological examination prior to allowing medication. No studies had been done to show differential stimulant effects based on these distinctions, which, of course, had no validity. The controversy was expressed in schools, in the mass media, but was not as nasty as it subsequently became. Although there was early hostility towards a psychiatric establishment viewed as controlling children's behaviour, later on the attacks became more systematic. At the same time, however, a constituency on the other side developed, such as parent groups. When we started, there was no pro-medication constituency.

Because of the climate, we decided that we would diagnose only children whose parents agreed with the school regarding the child's comportment. The reasoning was that, if children had signs of the condition in these two important functional settings, one could not really challenge the notion that they had a problem that deserved professional attention, and claim that the teacher was the problem.

Can you remember any early meetings or any particular kind of occasions when you realized there was this hostile point of view and that it was going to be an issue from here on?

I can't remember a point when the situation changed. It always was a problematic issue among those who argued that the disorder did not exist, those who argued that it was due to improper conditioning and that medications were undesirable, and those who felt that the disorder represented impaired function independent of specific environmental factors. Perhaps I'm missing the gist of what you're trying to get at.

No, it's just I can see that you are there seeing very good clinical responses, better than you saw with the other kind of conditions that you talked about, but yet you had to face the hostile public reaction that ADHD had triggered. I'm just trying to work out if there was any point at which you began to realize, well, that this wasn't just a minor public hostility, this was really serious business?

That's the feeling we're experiencing now. We didn't then. Although there were real objections, there wasn't this fervour about attacking psychiatric practice.

Let's put it the other way round. The first time I was aware of these views about Ritalin was from Peter Breggin

The first book I know of attacking the notion of diagnosing children with hyperactivity was published in 1975 by Schrag and Divoky, *The Myth of the Hyperactive Child*. It received a great deal of attention in the mass media, and was followed by similar attacks. Thus, as early as the early 1970s, there were passionate criticisms of medicating children, but it wasn't as systematic as it is now.

When did the contributions of Paul Wender and Judith Rapoport begin to play a part in all this?

Paul was a major influence from the beginning, with his book *Minimal Brain Dysfunction in Children*. He was not the first to express the view that these children had a biological disorder, but he did it in a very articulate fashion, and in a book. There was a dearth of literature in the area and his book filled a vacuum. His way of describing the children was simply wonderful, and the book gave terrifically compelling examples of the children he was talking about. An additional appeal of the book was Paul's theories of the types of neurochemical and psychological abnormalities in hyperactive children. He suggested that the children were resistant to reinforcement and therefore to corrective experiences because of abnormal dopamine regulation. These theories gave the field a scientific cloak that, at the time, made sense. I think Paul was very influential through his compelling observations and theoretical formulations.

I thought the work suffered from the weakness of not having enough empirical support – there wasn't a lot of evidence to support the theory. There were no abnormalities found on electroencephalograms (EEGs) etc., or, if there were, it was only in a small subgroup, and dopaminergic compounds were not the only effective ones. For example, phenothiazines, contrary to the stimulants, block dopamine activity. Yet they also work. It was difficult to get information to document the minimal brain dysfunction model. Things may be changing, but then, the theory was based strictly on the fact that stimulants had dopaminergic properties. It's rather simplistic: the stimulants affect the dopamine system, therefore that system must be deranged. Nevertheless, I think that Paul was extremely important in making people think differently about this syndrome.

Judith came on the scene in the 1970s. Her first study compared imipramine and methylphenidate. She became very productive and thoughtful in her attempts to pursue issues of associated central nervous system (CNS) development, such as minor physical anomalies, and other neurobiological models that could distinguish hyperactive children from others.

She did the work, though, showing a paediatric response, isn't that right? She, as I understand it, gave the drugs to either her own children or some of the other staff on the NIMH, showing that, even in children who weren't hyperactive, these drugs have a particular effect. Did that influence things?

She tested the notion of a paradoxical response in hyperactive children. However, if I may say, this was a single-dose study and you really can't generalize about the effect of chronic medication from a single dose. The fact that stimulants enhance attention in non-hyperactive individuals is not surprising. In fact, their effect was discovered through such observations in normals. The more relevant issue is whether, when given chronically, they reduce activity in normals, as they do in hyperactive children. We don't know whether the reduction in activity level would be sustained in normals over extended periods

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of exposure. It's a complex issue. The stimulants are excellent 'energizers,' or antifatigue medications. For example, it is well known that, during the Second World War, the Japanese army made extensive use of methamphetamine, and that this enabled the army to undertake extraordinary feats of endurance. These effects are not really compatible with a model that stimulants lower motor activity or have so-called calming effects. But Judy's study is widely quoted as putting to rest the notion that stimulants have a paradoxical effect on these children, and that therefore the children have a distinct physiology. That's important insofar as improvement on medication cannot be used as unambiguous confirmation of the diagnosis.

Did that play a part in legitimizing the entity? It seemed to be that, in some sense, you were putting a thing right.

Yes, and I think Judith's work made this view less tenable. Until then, people were claiming that these medications had specific effects in hyperactive children. There was some argument that you could use a response to stimulants to confirm the diagnosis in ambiguous cases. And now people were saying, 'Look, everybody gets better, so there's nothing specific about this diagnosis, and we are not dealing with a pathological entity'. I can't say Judith's work did this, but the notion that there was no paradoxical effect of the medication was viewed as very important. The same question led us to a study we conducted in the early 1970s, that aimed at determining whether the attentional effects of stimulant treatment were specific to hyperactive children. The issue was, however, who could one treat ethically with stimulants for any length of time? You can give one dose to normals, but it would be difficult to justify extended exposure. We could justify treating children with learning disorders, such as reading disorders, who had no behaviour problems. Based on systematic assessments, we documented that over 12 weeks of stimulant treatment their attention was improved, but their behaviour did not change. They did not become less active, unlike the normal children who had received one stimulant dose. If, in fact, there is no effect on non-hyperactive children's behaviour over time, then there is, indeed, a specific stimulant effect in hyperactive children. I don't think we can assume that anybody's level of activity will be reduced with stimulants, even though attention is enhanced.

When did you get to the point of doing long-term trials?

Obviously, long-term studies had to come after short-term studies. We have conducted two types of long-term trials. One is simply giving medication over long periods of time and the other is doing longitudinal follow-ups. As we've discussed, the whole field of treatment of hyperactivity has been extremely contentious. It's clear and dramatic that the medication works only as long as you give it. If you stop it, no matter how broad and effective the treatment has been, the effects are not sustained. This phenomenon led to devaluing stimulant treatment. There has always been the argument that 'it's not enough'. I don't know of any treatment that is enough for all patients. That's the sad part

of psychiatry, I guess: we don't have cures. In this case, medication was indicted for not doing everything. It was conceded that children were better behaviourally, which is what they were being treated for, but not academically, which is not what they were being treated for. People were always upping the ante while claiming that non-medical techniques were less deficient than stimulants.

So, with Howard Abikoff, we devised trials that attempted to address aspects of function other than primary symptoms of the disorder. At the time, the view was very vigorously promoted that hyperactive children suffered from metacognitive deficits – that they couldn't analyse problem situations appropriately, whether these were social, academic or other. We tested therapeutic interventions aimed at addressing these deficits. At the same time, we were convinced that you could not control children with hyperactivity without medication. Therefore, we compared adding ancillary treatments to ongoing stimulant treatment, since many stimulant-treated children have residual problems – at the same time, many do not. We did one trial in which we added cognitive training to stimulant treatment. It was a demanding programme in which children were seen several times a week for 4 months, and included training for parents to implement the programmes at home. Surprisingly, there was zero advantage of this ambitious programme combined with stimulants over using stimulants alone. These results were most disappointing.

We reasoned that perhaps we had taken the wrong tack in that we hadn't been strict enough in identifying children with clear-cut residual problems. So we undertook a second study, which was rigorous in selecting hyperactive children who, though they benefited significantly from stimulant treatment, had quantifiable residual academic problems. Even in this instance, the introduction of cognitive training added nothing to the medication effect. It's important to understand that we did these studies with a great hope of finding effective interventions. Earlier on, we had studied the effect of behaviour therapy compared to medication, as well as combined with medication in hyperactive children. We did not find any advantage to adding behaviour therapy, except in a few instances. I think behaviour therapy does have something to offer in addition to medication in difficult situations, but cognitive training doesn't. Yet, if you saw it in action, you would be impressed and seduced into thinking it is doing something important.

In the meantime, follow-up studies by Gabrielle Weiss and Lilly Hechtman in Montreal, and later by ourselves in New York, had revealed that hyperactive children have difficulty over time, and the field moved towards looking at whether one could modify their course early on to improve their long-term outcome. The next step then, with Lilly Hechtman in Montreal and Howard Abikoff at Hillside, was to develop a much more ambitious intervention for young hyperactives to supplement medication. We conducted a 2-year study in which family therapy, parent training, social skills training, individual psychotherapy and academic tutoring were administered. The treatment was individualized and efforts were made to address each child's difficulties. The

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treatment was very active for a year and continued in maintenance fashion for another year. There were two expectations. One was that, compared to children who received only medication, those who got medication combined with the enriched treatment package would be better at the end of treatment. The second was that they could go off medication more easily after a year of treatment because parental behaviour would have changed, and the children would have learnt all these wonderful social skills, etc. We found that there was no advantage to the combination of medication with the treatment programme over medication alone, and when children were switched to placebo at the end of the first treatment year, every one of them had to go back on the medication within a month, regardless of the treatment they had received. The same outcome ensued after 2 years. The results are not published yet.

So, none of our attempts to modify hyperactive children's difficulties with enormously costly psychosocial treatments paid off. But what we find is that we're on a slippery slope. It's a bit like psychoanalysis – it must work, and if it doesn't, it's because you didn't do it right. Others claimed that we didn't do it right, but they do. The multisite study sponsored by the National Institute for Mental Health (NIMH) took off where we left off. It tested a 14-month treatment programme, which was extremely ambitious; it included placing a paraprofessional in the school with each child for 3 months, a costly summer camp, plus parent training, and other interventions such as behaviour therapy. The study had the advantage of examining the impact of the psychosocial treatment alone, medication alone, and the combination. There was no significant difference between medication alone and the combination, in spite of the enormous effort that went into the latter. Medication alone was far superior to the psychosocial intervention alone.

The study had a very nice twist in that a group of children were randomly sent back in their own community for treatment, and those children did as well as those having the ambitious psychosocial treatment. The data have not been published, but presentations indicate that the community children, many of whom received medication, didn't do nearly as well as the children on medication alone in the study. That raises the question as to what happens to study findings when they're exported into the community. In this case, at least, medication management is not done as well in the real world as in research protocols. That raises an important problem of how to educate care providers to optimize children's care. My guess is that, compared to the study, the dose level used in the community was lower and compliance was probably worse, and therefore outcomes differed in favour of the study children.

Let me take you back to DSM-III. The process of trying to draw up the criteria for ADHD must have been an interesting one?

That's one of the more interesting things I've done. However, I was not prepared for the controversy that the DSM-III triggered in the profession. The animosity, the hostility, the pejorative attitude we encountered in the psychiatric profession were really remarkable.

What were the issues?

They varied with the group; in general, it was felt that classification without inferences as to causality was missing the boat. Most child psychiatrists had been trained in the psychoanalytic tradition, and were completely committed to it. The critics' opinion was that they knew what caused children's problems and were getting to the root of the difficulties through play therapy. Removing these aetiological concepts from the nomenclature was very threatening. If only we had their wisdom and their vast experience, we wouldn't be doing these terrible things!

We were attacked right and left. I remember going to a meeting of child psychiatrists in St Louis in 1976 or 1977 with Dennis Cantwell and Judy Rapoport to present the childhood disorders of DSM-III. We were nearly lynched. As we walked out, I turned to Judy and Dennis and jokingly said to them, 'You two have a lot to answer for. How did you ever get into this field?'. They proceeded to answer me in all seriousness, as if this was a legitimate question, giving all sorts of excuses for their being child psychiatrists, given how dismal the field was. There was no rigor at all and, worse, there was no desire for it. If you asked, 'What's the evidence?', it would be clear that the question had never occurred to the clinicians who criticized us. Even worse, they viewed the question with consternation and contempt. I found that very surprising. Perhaps I was naive. These clinicians felt that they had a way of doing things that was perfectly satisfactory. If you said to them that there's no reliability in what you do, that as a result the field had no credibility, it just didn't penetrate, it meant nothing. They didn't care about that. There was no rational argument possible.

There were also family therapists who felt, perhaps rightly so, that the DSM-III would change the field forever by averring that there were ill individuals. It was felt that if the DSM retained vague, imprecise, descriptive standards, you could incorporate the diagnosis into any theoretical framework, and the proposed DSM blocked that opportunity. From their point of view, social systems, not individuals, were ill. The DSM-III would shape people's way of looking at psychopathology in a way that would take them away from focusing on the family system. I think it's in part true, the DSM does shape people's thinking. There were many arguments. Bob Spitzer took a lot of heat. Eventually, compromises were made. If the document had been what it was originally intended to be, it would have been much thinner, and much more rigorous. The process became very political, and various constituencies had to be accommodated. In the end, after what appeared as hopelessly mired negotiations, accommodations were largely minor, such as including the term neurosis in parentheses after anxiety disorders. Initially, it had been dropped because it was defined by exclusion (psychosis) and had no descriptive content.

You mentioned Dennis Cantwell. What role did he play? My impression was it's more behind the scenes, being involved in the politics.

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I think you're right. I think that Dennis will be remembered especially as someone who fostered the field through his intense involvement and active training of young psychiatrists. He had great respect for research and for establishing practice from systematic studies. He was scholarly, and had an uncanny knowledge of the literature. Denny was then part of one of the largest child psychiatry departments in the USA (at UCLA) at a time when there were no research departments in child psychiatry. He had a lot of charisma and became very well known in child psychiatry, to which he was completely dedicated. There are people who commit themselves in a way that's so convincing that you pay attention to what they say. He was a very popular, wonderful speaker and that contributed to his influence. He had been trained in St Louis, which at the time was the pace-setting centre for diagnosis, with Eli Robins as head of psychiatry and Sam Guze and George Winokur in the department.

Which is where, in essence, DSM-III came from. Is that a bit strong? You just see them as one of the groups involved, do you?

The St Louis impact on the childhood section of the DSM was both direct and indirect. The indirect impact was through their contributions to the field. St Louis was where the Feighner criteria had been developed and Bob Spitzer had been greatly influenced by the Feighner criteria. We also all felt that Guze and Robins were on the right track. The direct impact came through Lee Robins, who was a key contributor to the diagnosis of conduct disorder. But they were not actually involved in launching the DSM, and by the time Dennis joined the DSM he was already in California.

As regards DSM-III, did Bob Spitzer figure that the same thing could be done for the child field as was being done for the adult field, or was he a bit unsure about how all that was going to work out?

I don't think that the child section of the DSM was given the same importance as the adult section.

While we're doing all the rest, we may as well do them, too?

Right. However, once it was explained that it was important, he never resisted and he gave it the same kind of attention and care that he did to the adult section, but perhaps with less passion, you might say.

As regards ADHD itself, were there any issues in particular when it came to clinical criteria for that?

Yes, not so much when it came to the criteria, but to what it should be called. Paul Wender won and I lost. Paul held the theory that the underlying as well as the manifest disturbance was in the attentional domain and that it should be called attention deficit disorder. Other influential figures in research also held the view that impaired attention was the central dysfunction. I felt that was a mistake, that we didn't know enough to assume that a specific function was central, and that the name should be exclusively descriptive. What got these

children into treatment was the fact that they were impulsive and hyperactive. I felt that the syndrome should reflect this clinical presentation and that we should not make any assumption about the nature of the pathology. The diagnosis of attention deficit disorder was adopted, and qualified as being with or without hyperactivity.

You would have called it what?

I would have called it hyperactive impulse disorder. There was a strong sentiment to change the name in the DSM-III-R, but the name was retained because of petitioning from paediatricians who desired to retain it.

So, in a sense, what Paul Wender achieved went against the grain of DSM-III, which was to leave any theoretical preconceptions out.

Right. But at a different level. In terms of the neuroses, the preconceptions involved intrapsychic conflictual and defensive processes, whereas here they evoked one aspect of the disorder as underlying all its other manifestations, much like Bleuler's notions in schizophrenia.

Paul Wender also introduced the idea, perhaps not at this point – you'll have to fill me in about when – the whole idea that the children don't grow out of this; that there may be a reasonably large proportion who, when they become adults, will still have some of the features of the condition at least. When did the idea that it's not just a childhood disorder come into play?

I think Paul is responsible for introducing the notion of adult ADHD. He was the first, really, to bring the adult condition to the field's attention. He didn't do follow-up studies of the children, and I'm not sure of the origin of his observations, probably from his clinical work. Having been sensitized to the childhood disorder, he could recognize it in the adults as well.

Roughly when did the issue of adults having the condition begin to come into focus?

It really came into focus in the early 1990s. Articles appeared in the literature, and clinicians gave talks about their personal clinical experiences. In addition, research grants were awarded for studies on the adult disorder. Paul Wender published psychopharmacological studies in adults and found, in one instance, that when the adult diagnosis was supported by parental reports of childhood hyperactivity, he obtained better results in a double-blind study than when he relied on patients' self-reports exclusively.

After the DSM-III criteria were put in place, things were, I guess, reasonably settled for a period of time. You had a real entity, which you could research and treat, but, as you say, in recent years the public profile of the area has begun to rise. It has all become a big issue. What's driving this? What's going on?

I think the mass media have a tremendous influence, both good and bad. Not long ago, it would have been unheard of to have parents come into your office asking, demanding, to get medication for their children. Now it happens often;

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at times you have to talk them out of it and suggest that we try something else first, etc. The term 'chemical imbalance' has gained wide currency among parents. TV shows, articles, books parents are great consumers of all these 'how to help your child' materials etc. I think parents welcomed the notion that they were not the bad ones. They've lived in a world in which they were guilty until proven innocent. And, in fact, they never could prove themselves innocent, no matter how compelling their case was, even in the case of infantile autism, a condition that is so blatantly neurobiological.

I think that's a great relief. I don't see parents abusing the new views – in the sense that now they are not willing to examine how they themselves can contribute to their children's progress. On the other hand, the attitude that parents are entirely responsible for children's difficulties is still very common. I haven't done a survey, but I would bet that it's still the most commonly held viewpoint in child psychopathology, at least by the public, and by many in the profession. When I was a graduate student, we used to joke that the question was not whether any one person had schizophrenia or not, but what kind of schizophrenia he or she had. Being able to perceive the underlying psychotic process was a sure sign of one's diagnostic acumen.

How do you explain the fact that it seems to be in the USA more than anywhere else that the ADHD thing has begun to roll, both from the point of view of the research and that you've more children actually being treated in the USA than in the UK, for instance, but also the controversy has been a much larger in the USA? Is there any reason why this is played more in the USA than in Europe?

The reason for the relatively elevated prevalence of treatment and diagnosis in the USA may be akin to the situation that had previously existed for manic-depressive illness, which was diagnosed much more frequently in the UK than in the USA. In the USA, schizophrenia was the rule. There was a vogue for seeing it under every rock. We even had the diagnosis of pseudoneurotic schizophrenia for patients who had no history of psychosis. In the UK, this was not the case. Schizophrenia was clearly distinguished from bipolar disorder, and psychiatrists used lithium, whereas they did not in the USA. The US psychiatrists, simply put, were off the mark. Having an effective treatment, like lithium, eventually called attention to the diagnosis. It now paid off to recognize manic-depressive illness, to make differential diagnoses, and made it easier to abandon the view that psychosis and disorganization were invariably linked to schizophrenia. Not every very disturbed, psychotic patient was schizophrenic.

I think the same situation has occurred in ADHD. In the USA, we have a wonderful treatment for it, so it makes sense to try to recognize the disorder. But it's a treatment the UK has never accepted. As a result, there is no specific intervention. If you can't do anything specific for it, you're not likely to attempt to ferret it out. If treatment is the same as for all behaviour problems, there is little point in trying to sort them out. Until the treatment situation changes in the UK, it's likely that the diagnosis will continue to be ignored. Now, why has it caught on here? I think it's because the work was done here. That's a real

issue. You know the expression NIH – not invented here? Unfortunately, I'm afraid there are still some territorial attitudes. The work has 'Made in the USA' stamped all over it. If there had been a body of work done in the UK, the situation might be quite different. Historically, there's been very little treatment research in child psychiatry in the UK.

Absolutely. Why?

I think the Maudsley has been a major influence in child psychiatry, and a wonderful one. It has made major contributions, certainly in diagnosis, in identifying relevant social factors through seminal epidemiological and longitudinal studies, in debunking much myth. I could go on and on about the incredibly important work done at the Maudsley, and elsewhere in the UK as well. But treatment seems to have been devalued all along. I don't know why. I think you would have to ask the leaders at the Maudsley who have shaped child psychiatry research. Somehow, there is this status thing about treatment research – that it's down the totem pole.

Why is that?

It beats me. Psychopharmacology has had a major influence on shaping views in the past 30 years in adult psychiatry. Theories of neurobiology have all emanated from psychopharmacology. And yet, in the UK, treatment in child psychiatry has largely been ignored. When it's done, it seems to be reluctantly. How do you explain it?

I think you're right that the Maudsley, for whatever reason, and it isn't only in child psychiatry, have not been enthusiastic about trying to advocate the use of any kind of treatment. But I think their influence in this regard in the child field has been even more pervasive. It's curious. Right, so how do you see the field going from here? Is it generally accepted now that it's okay to treat children with pills in the USA or are there wars still there that need to be fought?

I don't want to represent American child psychiatry because I live in a special world, in a psychiatry department that's dedicated to research, and where the influence of biological psychiatry is enormous. Perhaps I have an over-optimistic view of what's going on. Where is it going? I think the effect of biology is enormous. Genetic studies are taking off and there's very serious attention paid to the possibility of genetic transmission of various childhood disorders. Whether that will pay off or not in terms of practical consequences, I don't know. But there's the conviction that it has to.

I think that the numerous psychosocial treatments for hyperactivity that have been studied have been so disappointing that I can't imagine further research in this area, unless someone comes up with a very innovative plan, but I've been wrong before, and I may be wrong again here. We need longer-acting medications for hyperactive children. We know very little about the proper psychopharmacology of most childhood disorders. The studies are minute; there's virtually nothing on anxiety disorders; in depression it's not all that

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terrific. Here, I hope, there will be changes in the field. I view adolescent depression as a heterogeneous diagnosis – that's not a generally shared view and there has been very little attempt to test various notions that might distinguish clinical entities within the overall class of adolescent depression.

I also hope that the next DSM will bring greater precision to clinical terminology. Child psychiatry has become embroiled in controversies that seem due, in part, to the varied usage of diagnostic terms. Clinical features, such as grandiosity, mean different things to different people. A case in point is a current debate about the diagnosis of bipolar, or manic-depressive, disorder in children. Some claim that it's highly prevalent and that it is misdiagnosed as ADHD. Others, including ourselves, believe that the clinical concepts such as grandiosity are being applied in idiosyncratic ways, leading to diagnostic confusion. The future DSM will, I hope, minimize interpretational variance.

We really have very limited knowledge in child psychopharmacology. We will, of course, expand that body of knowledge. The movement is towards multisite studies. Right now, almost everything that is done has many participating sites, each contributing a few cases or a proportion of the study. I think that's fine for testing a treatment hypothesis. It's not so great for generating astute observations and hypotheses that lead to further work. There's something that's missing from these trials – you just don't have the same input by the principal investigator. They don't attract top clinicians to assume hands-on care of patients.

That's a huge problem with the whole field. Increasingly, very few leading people really run the trial themselves and get a good feel for just what's happening clinically. Now, having made that point, it's probably worthwhile to bring out that perhaps one of the good things you have had is that most of the trials that have been done in the child field to date have not been linked to industry, whereas the adult field is largely controlled by industry. So, in that sense perhaps, the findings you have look slightly better – in a sense of unbiased and independent – than the work from the adult field.

Yes, I agree, that's true. Until recently, industry has not been particularly interested in children. I think it's probably due to the fact that, in the USA, liability issues with children take on enormous proportions. However, there are now pressures from regulatory agencies to study children – another thing that does not hurt is that it has become good business, whereas it wasn't in the past. Childhood is a transient state, with a relatively small temporal window for treatment, and medication in children was very unpopular. As a result, the market value of a psychotropic product in children was not very favourable. That has changed with the recognition that there are a very large number of children with psychiatric disorders. The challenge for child psychiatry is to develop a cadre of experts who can go on and train young people. But how does that begin? How do you initiate that process? That's a major issue now. These medications are used widely but poorly.

What's going to happen to the opposition? Outside each American Psychiatric Association meeting these days, you have the Church of Scientology, and one of the things they will

always have their posters about is the use of Ritalin for hyperactivity. Is it just going to fade away, or are these forces going to be with us for some time?

I don't know what they have in mind or what their plans are. I don't know how important it is to their integrity or finances to keep picking on psychiatry. It's not clear to me why they've opted to do so. It's obvious that Ritalin is an easy target because it's used so widely. You're not going to attack something that's relatively esoteric, or unusual – the Ritalin issue is understood by everybody. Will that change? I doubt it. Right now in the USA we're going through a difficult period; it has become more difficult to do studies with children. It's not easy to identify what fuels these media-hyped fluctuations. Our society is extremely polarized and it's not likely that these controversies will end until we can demonstrate objectively that we're dealing with diseases. Short of that, I think there will always be those who have unreasoned, passionate objections to rational medical treatment.

My hope for the future is not too different from anybody else's hope. I think that we still have a long way to go for diagnosis to have the precision necessary to optimize treatment. Practice is vastly superior to the time when I started in the field, although it's hardly terrific now. But the changes are almost unbelievable. Better knowledge of the longitudinal course of various childhood disorders is needed – that's very poorly mapped out. The burgeoning of brain scans demonstrating abnormalities in many psychiatric conditions has been ideologically helpful in supporting the view that the brain has something to do with psychopathology and weakening the position that the disorders are in the eyes of the beholder. However, the treatment payoff is not imminent. At the same time, with growing specificity, child psychiatry will be more similar to general medicine diagnostically. That should translate itself into better treatments, and better understanding of the pathological mechanisms that are corrected with treatment. Much of what we do is still empirical. It's certainly better than nothing, but it's a far cry from the precision we hope for.

