GERALD KLERMAN & PSYCHOPHARMACOTHERAPY MYRNA WEISSMAN

Gerry's first contribution came with the Psychopharmacology Service Center study of chlorpromazine in the early 60s.

I did not know Gerry then so this is not first hand. I heard some of it when he died at his eulogies. Gerry was trained at New York University and then he went to Harvard for his residency. The psychoanalytic movement was very strong there then and he was trained as a psychoanalyst. He got an official certificate but he never completed his second analytic case so he wasn't considered a bona fide analyst but he certainly had extensive analytic training which in those days was very lengthy. He was intrigued with the ideas of psychoanalysis but he was intrigued with ideas in general. He finished his residency around the time of the Korean War and he opted to go into NIMH to do his military service. In those days it was called the "yellow" berets. He was assigned to work with Jonathan Cole, Chief at the Psychopharmacology Service Center at NIMH. Jonathan Cole was beginning the first multicenter study of phenothiazines in schizophrenia to establish if they worked in different settings and with different schizophrenic patients.

It was Gerry's job to help organise the Study. It was a natural fit. He was fantastic at administration and very interested in seeing that it was done well. He helped in the training of the interviewers at the different sites and establishing reliability. He was also involved in developing some of the assessments, especially the measures of social functioning. He felt that it would not be a great outcome if the symptoms of schizophrenia, the thought disorder and hallucinations, were relieved but the patient was sitting home contemplating the wall and was not working. He had the idea of quality of life as an outcome very early on. He worked with a young social worker, Eva Deykin and they developed social adjustment scales for schizophrenia which dealt with normal behaviors from brushing your teeth and dressing yourself, to going to a job.

After that he was invited to come back to Harvard to take a position in psychopharmacology and clinical psychiatry. There he linked up with Al DiMascio PhD, who was a young psychologist, also interested in clinical trials. They did a number of studies. They were not just testing drugs - they tried to answer psychoanalytic questions using research designs. Gerry was very committed to the idea that you could test most things if you could define them. For example, there was a theory that depression was "hostility turned inward". He tested it. He measured hostility in depressed patients before they had medication and then afterwards and concluded that depressed patients were hostile and irritable during the height of their symptoms but that this was part of the symptomatology generally and hostility diminished with recovery and thus depression was not hostility turned inward.

Can I take you onto the work with Gene Paykel on life events because that did two things - it led on to interpersonal therapy (IPT) and it also helped break down the idea that there were two forms of depression an endogenous unprecipitated form and a neurotic form that was a consequence of adversity.

Gerry was invited to come to Yale in 1965 by Fritz Redlich who was one of the most prominent psychiatrists in the United States at that time. Fritz was a force and an intellect, he was involved in the community mental health center movement and he was the Chairman of the Yale department at the time. In the following year the Mental Health Center was opened and Gerry was soon after appointed its Head.

Gene Paykel was a resident in England at the time and he came to see Gerry in 1966 planning the next phase of his career. It was clear that both of them were interested in the maintenance treatment of depression. At that time treatment approaches during the acute phase of depression were clear but Gerry was interested in how long the treatment should

be continued, whether continuation treatment varied by particular subtypes and also what was the effect of psychological treatment. He felt that psychosocial treatment should be part of any maintenance study because patients were receiving it anyway in clinical practice. The standard treatment for depression in clinical practice was psychotherapy. In fact there was a discrepancy between the treatment studies in depression which were on medication and the practice which was psychotherapy. The only psychotherapies which had been tested, and even then on small samples, were behavioral treatments and they were not used by psychiatrists - they were used by clinical psychologists who did not use medication. There was a real discordance in the whole field between the data and the practice.

Gene and Gerry designed the research protocol and Gene was offered a position by Gerry at Yale and they applied for an NIMH grant. First they wanted to estimate and describe the characteristics of depressed patients, so they surveyed all facilities treating depressed patients in the New Haven area. They were not community surveys but they collected data from hundreds of patients. As part of the survey they studied the nature of depression including life events, subtypes and medical history. The first papers on life events came from this survey. They looked at whether endogenous patients had life events and of course showed that they did. They showed that, as expected, hospitalised patients were more severely ill than non-hospitalised but didn't differ on the various subtypes of depression then in vogue - for instance endogenous or neurotic. They also showed that the endogenous depressions that were presumed to come "out of the blue" had as many life events as the neurotic depressions.

The original maintenance treatment study was designed with group therapy. The reason was they had experienced group therapy staff and they felt this was most efficient for the emerging community mental health centers. They wanted the treatment tested but it should be feasible to be used in practice for a large number of patients if it turned out to be efficacious. The NIMH study section approved the grant but they decided that group therapy was not easy to study. In point of fact patients were not getting group therapy in practice, they were getting individual therapy.

This was when I came on the picture. It was 1967. I was just out of school. We had just moved to Yale. I had four small children and I was looking to work 2 days a week at something interesting. I was told to go see Gerry Klerman, I would like him and like his ideas and he would be fun to work with. I went to see Gene Paykel first and we got on very well and he had me see Gerry. Gerry and Gene were willing to agree with my two days a week condition. In those days there was a shortage of social workers and especially ones interested in research and although I knew very little about psychotherapy or social work. They hired me to help with the study which would now have the psychotherapy delivered by social workers, until they found a senior social worker to be in charge of the psychotherapy.

Once a week, here and now as opposed to looking in depth at the past

No, the psychotherapy was just called high contact when I came on the picture - high versus low contact. Gerry may have had these ideas in his head but that wasn't explicit in the grant. It was going to be once a week versus assessments monthly. I remember the first day I came to work. There was Gene and Gerry and research assistants. My babysitter didn't turn up so my 18 month old was there too. I called Gerry in the morning and said I can't come to work I don't have any help. He said bring Jonathan. So I arrived at the first meeting, an interesting discussion about life events. The data were showing that there were more life events in depression before the onset of depressive symptoms compared to controls, but the events were just a laundry list and the question was how to categorise them. I remember Gerry saying it should be exits and entrances because exits would be more relevant to depression. They talked about factor analysis and cluster analysis. It was absolutely

marvellous. I had never been in discussions that were so interesting about a field that I knew very little about.

I worked with Gerry and Gene. Gerry was always into generating challenges. My first assignment was "design the psychotherapy". I had almost no experience and so what I did was to try to go back to first principles. He had said to me we know what amitriptyline will be like in Boston and we know it is the same in Boston and New Haven - we have to have the same assurance with psychotherapy. Thinking from first principles, therefore, the first hurdle was dose. The second should be the kind of people we hire so that psychotherapy is given in the same quality and the third, the hard part, was to figure out the content that made sense for depressed patients. What did I know from social work training? That's where the "here-and-now" focus came - that you don't want to undo people more by delving into past experiences that might be upsetting, that you help them deal with things in the present. Gerry gave me some papers he had written. One in particular which was written with Eva Deykin was on The Empty Nest - Psychosocial Aspects of Conflict between Depressed Women and Their Grown Children and another one was on the interpersonal dynamics of hospitalised depressed patients home visits. The point that he made was that depressed patients' symptoms could be exacerbated by what was going on in their interpersonal environment. In one of the studies they looked at patient symptoms changes when the family visited and there was a dispute and found that the symptoms returned. So although he believed that depression was a biological disorder, he saw the interpersonal context as very important to the onset and recurrence of symptoms which made a lot of sense when I was trying to design the psychotherapy.

I remember first developing a ten page description of "do's and don'ts" - you don't regress, there's no transference, no dream analysis etc. I tried to rule out the most obvious things it shouldn't be, hoping that what it would be would evolve as we got cases. I worked closely with Gerry on this. He was marvellous at taking what I was doing, conceptualising it and taking it to the next step. Gene at this stage was involved with the life events and in designing and managing the drug side of the study. Brig Prusoff was also hired at this point as the statistician. She was also just out of school but while inexperience she was very smart and welcomed the challenge.

At this stage the study had one site but Gerry had had the experience of collaborations and he felt that two sites would accelerate the work. So he submitted another grant with Al Di Mascio at Harvard. The NIMH committee requested a site visit to Boston. It was Gene, Brig and my first site visit. It was a heady experience to be reviewed by the NIMH but we got funded and we were up and running. They never hired the senior social worker who was supposed to develop and run the psychotherapy between the two sites. During the time both sites were going we had developed the first iteration of the psychotherapy, high contact - later to become IPT.

Soon after that I was assigned a second major task by Gerry which was to design the outcome measure for the psychotherapy. He said design a social adjustment scale for depression because that will be a major outcome. That was a challenge because I didn't have any background in social theory, sociology or psychodynamics - but his may have been helpful. I decided to see what had been done. I collected all the scales and I remember coming to work one day with a report which I called 'all you ever wanted to know about social adjustment scales'. That review later turned out to the paper called the Assessment of Social Adjustment which was used in part as an ACNP summary of relevant outcome measures for psychopharmacology trials and was later published in the Archives of General Psychiatry.

What was clear was that there were two types of social adjustment scales. There were the ones designed to assess schizophrenics which was work that Gerry had done at NIMH but the level of functioning assessed was too low for depression - we really didn't need to ask depressed patients whether they were brushing their teeth or bathing. The second were scales that had been developed by psychologists to assess College students in university settings and they asked a lot of questions about sex and dating. They were relevant but they still didn't assess important areas for depressed patients who were mostly women in their 30s and 40s with families and children. Gene had met Barry Gurland who was developing the SSIAM. Barry's scale was good, certainly better than what was available but it didn't have a scoring system, it was somewhat complicated and it didn't have measures for parental functioning. We invited him to come to Yale and talk about his work. We were impressed but in the end we started to work on our own social adjustment scale. We came up with something that seemed to make sense. It had social roles in it. The idea of conceptualizing roles as instrumental and affective was Gerry's -he had had a training in sociology.

Finally we had the first draft of the Social Adjustment Scale (SAS). Then he said to me "now you have to validate it". I remember asking "What does that mean"? He said you go out and get a group of non-depressed people and see if you can discriminate. Well that is very interesting, I said, where am I going to get a group of non-depressed people and he said "Go talk to Jerry Myers". Jerry Myers was a distinguished medical sociologist at Yale who had worked with Redlich and Hollingshead and had been doing studies of impairment in the community. He gave us some ideas about how to get a sample using the normal neighbour method - you select a depressed patient and then chose a neighbour ten blocks away, send an interviewer out to make sure they didn't have a psychiatric disorder and if they didn't we would interview them using the Social Adjustment Scale. We had a sampling method for who to approach if subject 1 was ill etc. and this method gave us a matched control. The result turned out to be the book The Depressed Woman, which I wrote with Gene Paykel, published by the University of Chicago Press.

By the time the book was finished we had some data from the maintenance study. When the study began I hired two senior experienced social workers to do the clinical work. Gerry and I and the two of them would meet once a week and discuss cases. That process helped us to refine IPT, which we developed through this iterative process. In 1970, Gerry left to be Professor at Harvard and run their new mental health center. Gene returned to London in 71. I went to graduate school at Yale. I would have been happy to work on that team for the rest of my life because it was so interesting. I wasn't thinking of a career but I said if I want to continue the work I'd better learn how to do it myself, because both Gerry and Gene had left, so I went to Yale to study epidemiology.

I still continued working with Gerry on the studies. The grant was transferred to Harvard with Gerry as the P.I. subcontracted to Yale. We started to analyse the data working with Gerry, Brig Prusoff and Gene in London. Gerry didn't think psychotherapy would show an effect. There was no reason to think it would show an effect - there had never been a positive psychotherapy study but there also had not been many studies. But, he said, if we show an effect it will be on social functioning..

Was this the Parloff-Frank idea that drugs act on the symptoms of depression and psychotherapy acts on the social adjustment.

It could have been. Gerry was very impressed with Parloff and Frank. He thought that behavior therapy, cognitive therapy and IPT had some differences, so he wasn't convinced about the non-specificity argument. He had an open mind. Some time later when we had got further on in IPT he showed me a type-written manual that Beck had done and he said "We need a manual, like Beck is doing. You've got to specify the therapy. It can't just be a

black box, you can't just say be supportive. You've gotta say what you do to be supportive. I want scripts, I want examples. I want somebody to be able to pick it up and be able to figure out what to do and what to do next". I said "oh you mean strategies" and he said "right not theories but strategies and scripts". So we wrote the manual and as the therapists were bringing in patients we wrote the scripts. I didn't see patients because I wasn't experienced enough and he said we would have to have experienced clinicians because we wanted a bias in favour of an effect, so that they can't say 5 years from now that you didn't find an effect because you didn't have experienced therapists. He really had no ideologic bent on this. He just wanted accurate, unbiased results based on a good design - he and Gene spent hours on the design.

It was around that time that he wrote the paper on psychiatric ideologies and what comes through from this is that he had no prior commitments to a particular area. Yes. He wanted to know what the data showed and ensure it was analysed correctly. He said you can have any hypothesis you want as long as the hypothesis came first. If it came afterwards you had to be clear that it was post-hoc. That was what was so much fun. You felt that you were exploring and that it wasn't to prove a point. He expected psychotherapy not to work but he said we have to be sure that we're measuring what we think we are supposed to work on. He did say that psychotherapy wasn't going to make you sleep better but it should help you take care of your children and get along with your spouse better. At one of the eulogies for him, I quoted from the Osheroff case where Gerry was called a foe of psychotherapy and then I quoted from elsewhere where he was called a foe of pharmacotherapy. You really didn't know which way he wanted the study to come out, except that he wanted it to be a good study and considered a landmark. He said if it angered both groups it would probably be good. We were outsiders in the department, which was then strongly psychoanalytic. They couldn't care less about what we were doing. We were off in a little house outside the Department.

When did you become aware that IPT was working

When we analysed the data. The first thing we did was to look at relapse rate - that was the hypothesis in our grant - and there we showed very clearly that drugs had an effect on reducing relapse rate and psychotherapy didn't. Gerry was also way ahead of his time on this - he had said before we did the analysis that we had to define relapse. This was years before more recent efforts. Then we looked at social functioning and there we showed that there was an effect of psychotherapy on social functioning. That was what we had hypothesised. When we looked at the combined drug and therapy group, we showed that in the combined group you would get the best effect because the drugs worked on symptoms and therapy on social functioning.

Then he said we had to do a follow-up, so we did 6 and 12-month and 4 year follow-ups and that was my dissertation. They wouldn't let the Depressed Woman book, which I though was more interesting, be my dissertation because I began it before graduate school. But I did learn a great deal about follow-up studies from doing the dissertation.

Gerry felt that we could get a stronger psychotherapy effect with a different design. In the maintenance study the patients had to first respond to medication. Therefore we should go back and see if there was an effect of psychotherapy on acute treatment. By that time Gerry was in Boston and so it was a Harvard-Yale collaboration. He designed the acute treatment before he left for Boston and he was the Pl. He subcontracted the acute treatment study to us at Yale and we carried it out with regular meetings of the team in Sturbridge Mass - about half-way between Boston and New Haven. We completed the acute treatment study in the mid-70s. The data paralleled the maintenance study to some extent but the effects were somewhat stronger, showing that drugs worked faster than IPT but by the end the effects of

drugs and IPT were equal and the combination was the most efficacious. This study went easily. We firmed up the methods of IPT, got more cases and wrote the IPT book from it.

Had High Contact become IPT at this point?

The book was published in 1984. We started working on it after 1974 when we had two trials showing efficacy. People were very interested in our approach and we were distributing a xeroxed manual which was fairly big at that point. We started to look for a contract - it was between John Wiley and Basic Books and we went with Basic Books because Jane Isay was working for them. By that time we had a couple of chapters that described our concept of the interpersonal approach to depression and when we got a contract we started to write the book. I invited Bruce Rounsaville and Eve Chevron to join us because they were therapists on the IPT acute treatment study and they provided us with all the clinical material and the scripts. Gerry provided the theoretical underpinning and I orchestrated the whole thing and made sure the work was done and that it made sense as a whole. That book is still selling and I have a contract now to revise it working with John Markowitz who was one of Gerry's students at Cornell. Now of course there are many adaptations of IPT and many more trials and that will all be in the new book.

IPT is now part of the APA guidelines for the treatment of depression in primary care. The official guidelines all came several months after Gerry's death. He would not have anticipated it. He would have been amused and alarmed that IPT was getting this much attention because during his lifetime it didn't get that much attention. There were many more behavioral and cognitive therapists and they were much more active than we were. One of the reasons we weren't active and one of the reasons we held back the book was because Gerry said until we had shown that IPT worked outside its own home-grown place we shouldn't go out and proselytise people. But by that time the Kupfer-Frank and NIMH studies were coming and it looked like it really did work beyond Harvard and Yale. On the other hand we really didn't want to set up training programs ourselves as it would have taken time away from research.

The reason it has gotten the attention I think is because in fact in clinical practice this is what is mostly done - a supportive here-and-now therapy. It takes more training for a psychiatrist or a social worker to learn cognitive or behavioral approaches because these differ more from what they actually do.

Around 1969 and partly because he was perceived as being acceptable to the social side of psychiatry, Gerry got involved in the NIMH Psychobiology of Depression Program. Two things came out of that it seems to me. First this was the occasion for him to coin the term neo-Kraepelinian. Now while people think of the neo-Kraepelinian school as being Eli Robins and Sam Guze, it seems to me that it took a certain political input from Gerry to get that bandwagon rolling

The Williamsburg meeting organised by NIMH in 1969 was a key meeting. That's where these notions that the classification of depression should be based on empirical evidence were presented. Gerry had been working on these ideas for at least 10 years - trying to have an empirical basis for some of the old concepts in psychiatry. He liked the idea of collaborations and he already completed the Yale hospital survey and used the data for studying different subtypes of depression. He was also very impressed with Eli Robins and Sam Guze and their paper on how to validate a diagnosis. He said that's what we need to do for depression. However he was not chosen to do the work because he was 'perceived to be acceptable to the social side of psychiatry'. He organised a group of investigators in 5 centers from Harvard, St Louis, Columbia, Rush in Chicago and Iowa and NIMH. He and Marty Katz and several others then wrote a grant and submitted it to NIMH to study the psychobiology of depression that would have two components - a set of biological and a set of psychopathological, clinical and epidemiological validators.

He was the person who brought Bob Spitzer in on this

Yes and in fact the SADS came out of this. Bob had been working on the PFF and PSE diagnostic assessment with Jean Endicott at New York State Psychiatric Institute. Marty Katz who was in charge of the Branch at NIMH said that they needed to have a structured diagnostic interview and he invited Bob and Jean to join the group. Eli Robins and Sam Guze's idea was that you had to have precise definitions and for this you needed a way of getting precise symptom data and that became the Schedule for Affective Disorders and Schizophrenia - the SADS.

One of Gerry's great strengths was that if he had an idea he could pick talented people to get the work done or sometimes he would take ideas that other people had and reformulate it into a broader perspective. For example, the application of life events to psychiatry originated in 100 Park St. Gene then took it up and ran with it and he did a fantastic job. The same was true with social functioning. It was Gerry's idea to assess social functioning but he was happy to have me carry it forward. He could fertilise new ideas or reframe old ones.

There's a story with the SADS which might be of some interest. I finished my PhD at Yale in 1974. By that time Gerry was at Harvard. I was working with Jerry Myers. Gene had started the collaboration with Jerry but he had left. Jerry Myers was going into the field to do the third wave of the New Haven survey on impairment which he had begun with Hollingshead and Redlich. He asked me if I would like to work with him. We were going to look at depressive symptoms - the CESD had become available. We got the grant for the study but I was dissatisfied. I knew that there were no rates of psychiatric disorder in the community there were rates of unhappiness or of impairment etc. There had been the mid-town Manhattan study which showed that 87% of New Yorkers were impaired - it was called Manhattan madness. So even if we used the CESD, which measured depressive symptoms this was not the same as assessing clinical depression - you wouldn't put people with symptoms on a tricyclic without knowing their diagnosis. I also wanted to know the rates of panic and GAD etc. I had heard about the SADS from Gerry so I convinced Jerry Myers to include it in the survey. It would be good to know the data on diagnosis and it wouldn't hurt his study, so he said fine. We would never have been funded to do a SADS study because the conventional wisdom was that you couldn't make diagnoses in the community - people wouldn't answer the questions. I called up Bob and Jean and asked them whether I could change their instrument, the SADS, which covered a 5 year period so that it would cover lifetime. They said they'd be happy for me to use it but they'd mind if I did it - they'd do it. I convinced Jerry Myers to hold up the study 6 months while they finished the SADS. They would send me pieces of it as they got it finished and we would try them out.

The New Haven study became the first study to look at psychiatric diagnoses in the community, using the same criteria as you would use in psychopharmacology trials and clinical studies. That study had only 511 people but it was the first community based rates of major depression, panic etc. Gerry had been appointed by President Carter to be Head of the Alcohol, Drug Abuse and Mental Health Administration. The President's Commission on Mental Health with Rosalyn Carter had been formed. Califano was Secretary of Health, Education and Welfare and he said if we are going to meet needs, he wanted to know how many people have needs. Gerry asked me for the data on diagnosis from the New Haven survey and I was sending him the data as we were getting it out which he then handed to Califano, showing what the rates of the disorder were and how many people who had disorders were getting treatment. After that the whole mood of the Commission was that we need to do an epidemiologic study and the people who said you couldn't do it could be argued with because we had done it. That set the stage for the ECA and then of course now

the CIDI and the National Co-morbidity study. These methods have been adopted all over the world.

The fact that he brought in people like Bob Spitzer and they produced the RDC, which was the prototype of DSM III, meant that by the time Bob Spitzer was hired to do DSM III in essence a lot of the work had been done

A lot of the thinking but not the work and much of the work that had been done had been done by Bob and Jean and later Janet Williams. Bob did a phenomenal job. He also took the position as well that you could define quite precisely the symptoms and that you had to have some consensus from the field as to what should symptoms should count and that there should be an empirical basis for making those decisions. Some of that empirical basis came from the ECA and the Psychobiology Studies.

In the 5-center study, the idea was to follow Guze and Robins' ideas on validating a diagnosis. To do this they included family history, longitudinal and biological validators and it began with precise diagnoses. Jan Fawcett, Bob Hirschfeld, Marty Keller, Jean Endicott Sam Guze, Nancy Andreason, Ted Reich, Bob Cloninger and others worked on this study which brought depression to the forefront. It provided a lot of information not only on subtypes of depression but on its clinical course. There is now a whole background of information on depression, which we now take for granted, but which was really not known when we started out.

Coming back to RDC and DSM III, while Bob Spitzer was clearly the co-ordinator of the whole thing, when there was a debate at the APA in 1982 or thereabouts about the merits or otherwise of DSM III, as well as Bob Spitzer, Gerry was up there arguing the case. Really he did as much if not more than anyone else to push it, how important was it to him?

I thought it was very important to him. Not because it was truth but because it provided a hypothesis for empirical testing. He felt it would need to be revised. But at least the script was out there in public and people can challenge it. It was not just an intellectual debate, you could actually do studies and test out hypotheses. Again he wasn't looking for truth, he was applying scientific methods so you could find out what was more likely to be correct than not correct. But the DSM III was Bob Spitzer's, he did it with passion and great intellect. I think DSM IIIR came too soon. People were just absorbing III. As an epidemiologist it was a pain in the neck having to switch criteria. Since these things aren't truth, they're constructs that allow you to get towards what might be more true than not true, I think it was too soon to change it.

How close was the relationship between Gerry and Bob.

On a working basis, Gerry worked more with Jean Endicott than Bob because she ran the Columbia site of the Psychobiology study. I wouldn't give Gerry the credit for doing DSM-III, I would give him credit for pushing the concept of an empirical basis to diagnosis and precise definition using methods proposed by Guze and Robins.

Coming to the President's Commision, a few things stemmed from that period. One was the ECA and another was the NIMH comparative studies of IPT, cognitive therapy and imipramine - what was his role in getting that off the ground in terms of work behind the scenes to make sure it happened.

He had become the head of the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) and the President's Commission was set up under Carter to look at the unmet needs in this country for people with mental illness. So in his position he had a major role on the President's Commission and he supported the notion of epidemiologic studies to establish baseline data. He had also been very keen on comparative treatment studies to be done. There was already evidence for the efficacy of cognitive therapy and for IPT worked

and considerable evidence for the efficacy of psychotropic drugs in the treatment of depression. So it was important to figure out what worked on whom and what didn't work and also to replicate findings. Gerry was a consultant to the NIMH on these issues before he went to ADAMHA and was advising on the design of the multicenter study. But once he became head of ADAMHA, he could not influence the study and he dropped out of any decision making or consulting role.

How did he take to his period in government?

Gerry considered the period in Washington the height of his career. He loved it. He was very proud of the fact that he initiated a very strong WHO-NIMH collaboration, aimed at harmonising DSM and ICD. I was in the room when the ideas for the development of a common assessment instrument, which became the CIDI, took hold. It was in Paris at Pichot's hospital, the Salpetriere. In the room was Bob Spitzer, John Wing, Lee Robins, Gerry, myself and some others. Gerry brought us together because he thought it was ridiculous to have international wars over the two classification systems and besides it was important to know what the disorders were in different countries and whether they were stable and consistent across cultures.

The discussion was that we needed a common instrument because the Europeans couldn't be expected to adopt DSM-III or the Americans to take ICD but that there ought to be a way of cross-walking the results of studies. In fact if you looked at the components of the disorders, the symptoms, they weren't that different. So Gerry got John Wing and Lee Robins to agree that they would put the PSE and the DIS together into an assessment instrument that would be able to generate ICD and DSM. From that effort the Composite International Diagnostic Instrument was developed - the CIDI.

Gerry was asked to stay on at ADAMHA and he agreed to stay until the election but he had no intention of leaving academia and of being a permanent government employee. After the election in November, he left in December. The outcome of these collaborations he had set up, ten years later was ICD-10, which is very much closer to DSM-IV and vice-versa. This was helped by Norman Sartorius who was head of the Mental Health Directorate of WHO - he and Gerry were close and respected each other. The combination of this effort and the fact that the younger generation involved with the Cross-National treatment study which he directed using DSM really helped bring the international community closer together.

He had a role in implementing the recommendations fo the President's Commission on Mental Health, which led to a Bill..

Yes, the commission report submitted to Carter in 1978 stressed a number of things - greater attention to the needs of the poor, greater support for research, support for clinical training, better third party financing of mental health care and increased attention to epidemiology and prevention. The team assembed to implement the recommendations were Califano, the Secretary of State, Don Kennedy who was head of the FDA, Gerry as head of ADAMHAand Herb Pardes who was recruited by Gerry to direct NIMH. Gerry led a government task force which submitted a draft bill which was accepted by the administration in Spring of 79 and presented to Congress on May 15th 79 with a special message of support from the President. After much debate the Mental Health System Act was signed in September 1980. While the Reagan administration dismantled much of the bill, certain parts of it remained, such as increased support for research, increased focus on epidemiology and prevention and a greater coming together of advocacy groups and citizens groups which remains even to this day.

You mentioned that he really had the intention to pull people together - because this is what he writes in the arguments with Isaac Marks over the alprazolam studies. Some people might see that as post-hoc rationalisation.

That's ridiculous. Now its obvious, but you have to remember he did all this work before ICD-10 and DSM-IV. He started the WHO-NIMH collaboration in 1977. People often don't recognise what he did because he would do something and then move onto something else. He loved the ideas and the chase. He was not a self-promoter. He got restless after the initial ideas took hold and were on their way to being worked out.

Can I take the alprazolam studies and the concept of panic disorder. When did Gerry get interested in panic disorder and why? Were the Upjohn studies a vehicle to run a large multicenter, multinational study which might show that DSM-III could be used outside the US.

One of the major outcomes of the alprazolam studies was that it created a generation of young investigators thoughout the world who had used DSM-III and who could talk to each other in the same language. A major outcome for me was that this generation of young investigators, some of whom did epidemiological work made it easy for me to get access to form the Cross-National Epidemiologic Group. The drug study was a minor outcome although it was very interesting in its own right.

Gerry had always been interested in anxiety, some of his early papers were on the relationship between anxiety and depression. He also had a great deal of respect for Don Klein. Don, in his APPA presidential address and in his book Anxiety Disorder Reconceptualised, revived the notion of panic disorder which had been very well described by Freud and forgotten. There had also been studies from the Washington University group on the biological basis for panic - studies on CO_2 precipitation of panic had begun to come out from there. Gerry was impressed with that symposium. The ECA study also provided data on the epidemiology of panic disorder and our family study showed that panic disorder plus depression had the highest familial loading. I didn't have a sample of panic only probands, so we didn't know whether this was because they had two disorders or whether there was something special about panic disorder. So we were all getting more interested in panic disorder and then alprazolam came out. When you have a treatment for a disorder it becomes more interesting and more visible.

How much did he feel or worry that panic disorder was something that Upjohn were just using to market a drug

I can't speak for Upjohn but the data on panic was available before Upjohn's study. Don Klein's work was there way before Upjohn and alprazolam. And there had been the studies at Mass General by Jim Ballenger and David Sheehan which had showed that patients with panic disorder responded differently to treatment than patients with GAD. Gerry had worked with both of those men at Harvard. He felt panic disorder was a real entity. I don't know what Upjohn's thinking was. They felt they had a drug which worked for panic where the other benzodiazepines didn't. So there was family data, there was epidemiologic data and there was some psychopharm data suggesting that panic disorder was different from the other anxiety disorders. It was interesting, that was his thinking.

I actually introduced Gerry to Jim Coleman from Upjohn when Gerry returned from Washington to Boston. I was at Yale and Boris Astrachan, who was head of the Connecticuit Mental Health Center, asked me to meet with the Upjohn people who were interested in running clinical trials in depression. I was running the Depression clinic at Yale but we had a study going and could not undertake another one then so I told them they should talk to Gerry Klerman. Gerry was interested at the time in designing a drugs and psychotherapy study to follow up the NIMH Collaborative study. The data on the efficacy of alprazolam in panic was coming out and Upjohn said they were interested in running a multisite study and invited Gerry to run it. Gerry laid down the conditions, there had to be joint training, inter-rater reliability, monitoring and a quality assurance team and Jim agreed and that's how they set up the studies.

First they brought a number of investigators together from the United States, Canada and Mexico. Then they decided to broaden it to Europe. They had a meeting in Key Biscayne. Giovanni Cassano, Sir Martin Roth, Max Hamilton, Don Klein and others were there to discuss the concept of panic. There was a lot of debate. The Germans said panic didn't exist and a lot of the Europeans felt it was a figment of the imagination of Upjohn to sell alprazolam. Gerry got Upjohn to fund studies to see whether if using DSM III criteria it did exist in European clinics. I remember Wolfgang Maier MD from Germany, who did one of these studies coming to the World Psychiatric Association meeting in Vienna in 1984 reporting the survey result. He had found panic disorder in non-psychiatric clinics. Because of the whole history of abuse of psychiatric patients in Nazi Germany, patients didn't go to psychiatric clinics unless they were really sick and people with panic disorder would be seen in non-psychiatric clinics. Although some of the older generation had been skeptical, now they had data.

I was part of the international quality assurance team and we saw patients with panic disorder in many different countries. It was the same disorder. Cultural context might be a bit different but I saw the same syndronme in Rio de Janeiro, Cali Columbia, Madrid, Barcelona, Toronto, Montreal, Paris and Pisa. It was the same panic. That's why my genetic studies are on panic disorder and not on depression - the epidemiology of panic is much more consistent across countries - the prevalence, the risk factors, the age of onset are similar and the family studies show enormously high familial loading - 7-fold - which is much higher than in depression which is only 2-3 fold.

Gerry did not analyse the alprazolam data. His job was to organise the sites and to see that the psychiatrists were trained and that the quality assurance was done. We visited each site twice and that was very important to ensure that the same patients were being entered at each site. He also convened the meetings so that the data could be presented, so for Gerry it was a lot of fun.

Until the end when the controversies blew up with Isaac Marks, that can't have been much fun...

That wasn't fun but Gerry knew where that came from. Isaac had a very strong ideological bent. If alprazolam didn't work it wasn't going to be any skin off Gerry's teeth because the major work for him was defining the psychopathology of panic working with a group of investigators, which was very intellectually interesting. If the drug was efficacious, that was nice, you like to have a positive study but it wasn't going to change his career.

I was so glad that many of the things that were said were said after he died. A book came out by Peter Breggin, Toxic Psychiatry, in which he said that Gerry got \$1 million from Upjohn for doing this study. I wish that were true. He was paid as a consultant but it was a relatively modest sum and the study took a lot of his time and energy. Gerry was not very motivated by money. And because he was paid as a consultant he could not do the study, so there was no site at Cornell and he didn't analyse the data.

What about the correspondence with Isaac in the British Journal of Psychiatry Gerry died April 3rd 1992. He went into the hospital the day before with a high fever. When he was going in he said to me "take a look at the letter on my desk, its my response to Isaac Marks' critique of our study". It had been looked at by all the investigators and he said "see what you think, I was going to send it on". He died the next day. When I came back from the hospital I looked at the letter and I looked at his response. Marks comments on the Cross-National study were inaccurate. I said I'm not going to let the record stand on that, this letter has to go out clarifying Mark's inaccuracies. I sent the letter around to all the Cross-

National investigators for their final approval. Then after I had their signatures, I sent it to

Hugh Freeman, the editor of the British Journal of Psychiatry. It was published but it was published with only Gerry's name. I had everybodys signature there and I felt it had less impact with only Gerry's signature - a letter from a dead man.

Is there a sense in which Gerry and Isaac were very similar people. They had both participated in the development of therapies - therapies which were the opposite to the corporate therapies such as analysis or even cognitive therapy. These were therapies that were easy to do, almost easy enough for people to do for themselves and as such very available. They were both interested in evidence-based medicine before it was fashionable to be interested in this. Both were forceful people who tended to appeal to the data.

Personality-wise they were different. I don't think Gerry was an ideologue. For him it wasn't either drugs or psychotherapy. He thought it was great that both could work because people respond to different things. Also Gerry had spent more of his career testing psychopharmacologic drugs and in encouraging studies of combined treatment. Isaac will have to speak for himself but I believe that he has more of a bent on psychotherapy. Gerry didn't develop a training program for his psychotherapy and its only now that IPT training programs are coming out of a groundswell. He wasn't out to proselytise people to do IPT. He was interested in it as an intellectual activity.

He was good at the apt phrase but the apt one here was "pharmacological Calvinism".

That was a great phrase - 'anything that made you feel good must be bad'. He said that this persisted today with the under-prescribing of drugs. But he was keen for both psychotherapy and pharmacotherapy to be utilised, he just thought treatment had to be tested. He always felt that there should have been a psychoanalytic study. He was very disappointed about the claims made for psychoanalysis because they hadn't been tested, it was not that he was against psychoanalysis.

That leads nicely into the Osheroff case. How did he get involved in the case? He was invited to be an expert witness for Osheroff and so he reviewed the material. He was often asked to be an expert witness but he didn't do it everytime he was asked because he was a busy man. When he read the case, he was appalled. This man had lost his wife, his children and his practice. He had been hospitalised for so many months without effective treatment and it was so clear from the records that he had an agitated depression. His feet were bleeding from pacing up and down so much. This history is a matter of public record.

He felt it was a very important case and from that case he developed the idea of the patient's right to effective treatment. The evidence was strong that drugs work for psychotic and agitated depression and that psychotherapy alone was not the treatment of choice. Drugs and psychotherapy would be good. Gerry never advocated not using psychotherapy.

There was a funny story which he told me about the case. He was being cross-examined by the defence's lawyers and he was asked to talk about what was the right treatment for Osheroff. He stated that the patient should have been on medication and when in fact he was transferred and put on medication he did well. Then the lawyer asked him "What about the writings of Weissman, who said that psychotherapy works as well as medication and found no difference between the treatments, in her study"? He smiled and he said "if you read Weissman's papers you'll see that she also shows that for delusional psychotic depression psychotherapy alone was worse than placebo". The lawyers had not done the homework or they would have seen that Gerry and I had published these papers together or that we were married. Osheroff came to Gerry's funeral and I met him there - I had never met him before. He was very grateful to Gerry. I tried to locate him afterwards but I couldn't find him.

After the case there was such a barrage against Gerry. There were the letters from Alan Stone. He was the most eloquently negative and of course he was a lawyer. That case in fact has made the legal journals and textbooks. Gerry's son Daniel, a lawyer and historian, pointed them out to us when he was a student.

Well there was a correspondence in the American Journal of Psychiatry with Alan Stone which is absolutely fascinating. Gerry was clearly in favour of guidelines, the regulation of psychotherapy and the need for evidence-based medicine etc before these things were fashionable.

Oh yes, he would love what's going on now except he wouldn't have liked managed care because it takes the control away from the physician using his best clinical judgement. He died before the guidelines came out recommending IPT. He would have been surprised at that.

Did the exchanges with Alan Stone become heated. One of things Michael Shepherd says Gerry said to him just before he died was that he had felt he was out there on his own and he felt let down to some extent by other people within the profession.

I can't say that. I think he liked the opportunity to debate the issues. He loved the intellectual duelling and he didn't take it personally but I think he felt that some of the things that were said about him were totally unfair, that he was against psychotherapy for instance when he had developed a psychotherapy. He felt that was unfair and personal. But he felt he was on stronger ground than anyone attacking him who were basing their position on their opinion whereas he had data.

Was there any animosity to him for saying things like there was a need for guidelines, which can be seen to be restrictive.

Sure, there was hostility. He respected Alan Stone but he just thought he was wrong. I'm sure he didn't like it but he couldn't resist the challenge and he wouldn't back down on what he thought was right. He did it because he believed in what he said and he believed it was in the best interest of patient care. He always kept a small patient practice because he liked treating patients and he felt it kept him in touch with where things were.

What about the area of the regulation of psychotherapy, which he was one of the first to raise

Yes. He spent a lot of time in the Hastings Institute. It was a think-thank that was interested in medical ethical issues. Will Galin was there and Perry London and Sisella Bok who wrote on ethics. So they had quite a heady time talking about issues. Perry London, who has since died, was also interested in the ethics of psychotherapy. Perry was a psychologist who did behavior therapy and wrote textbooks on it. The two of them wrote a paper on whether there should be an FDA for psychotherapy. They felt that psychotherapy wasn't regulated as to how many trials you needed and what kind of trials you needed before you could make claims for efficacy. It wasn't regulated as to who could do it, what credentials they should have etc. They weren't against psychotherapy but they felt that this was not a good situation for patient care and they were concerned about the ethical issues involved in uncontrolled psychotherapy. The Osheroff case fit in with his notions about the ethical issues in treatment - the importance of what is effective etc. He was way ahead of his time.

You could make the argument that we shouldn't have an FDA for drug treatment - that it forces a certain corporatism on the field by raising the hurdles over which people have to jump. He raises this issue himself when he asks who should regulate the field.

He thought it should be an independent body, that the profession should regulate itself.

But if you go down that route you end up forcing a corporate development because you have to have people organised to provide the proof - I would think that you necessarily end with a situation where some group like clinical psychology will take on cognitive therapy and because they make the investment in it they push the product whereas other groups like IPT or behavior therapy may not do so well even though the evidence for them may be better because there isn't a comparable group to push it.

At the moment there isn't a product in psychotherapy that some corporation is selling. This could change because some of these medical information companies are taking on the psychotherapies as part of their disease management. Corporate means "for profit" but these things don't have to be set up for profit. An FDA for therapy could be set up not for profit but so that people get efficacious treatment. I don't think its simple but I don't thing its undoable.

There is no industry taking the testing of it through successive stages. Most psychotherapies get put on the market before they are ready - in a way that would be like taking a drug from phase I studies and putting it straight onto the market. It should be tried in out different situations and there should be studies to find the right dose and then it should be tried against placebo. By the time a drug gets to market we know a lot about it. Psychotherapies don't work that way because no-one is funding phase 1 and 2 studies. The NIMH Collaborative studies and the Kupfer-Frank studies were what you might call phase 4 studies. Gerry did discuss this at the Scientific Board of NIMH, just before his death, and there is a mechanism now for getting small amounts of money for phase 1 and 2 studies in psychotherapy.

The first time I became aware of your work was in the early 80s and the piece that comes to mind is a chapter from Psychopharmacology the Second Generation of Progress, I think, where you had a piece that at the one time seemed a strange combination of the blindingly obvious and the utterly revolutionary - in essence it was making the case for a combination of psychotherapy and pharmacotherapy. This seemed obvious - perhaps more so from a European perspective - but in American terms was clearly revolutionary in that there was a tradition of just not mixing the different modalities of therapy. What kind of feedback did you get on that.

That was the one that had the quote from the Revd Baxter in the 17th century that in the treatment of melancholia you need psychic and physic. I was so unimportant a figure then - when I wrote the chapter in the 1970s I was still in graduate school, so I could just be ignored. But I was honored to be invited to present it at the ACNP.

IPT differs from cognitive therapy in making an explicit space for the biological aspects of depression and therefore making it possible to consider using both together. While Aaron Beck and John Rush originally maybe made some accomodation clinical psychology has since taken CBT up and the focus has been very heavily on the abnormalities of logical thinking and how could a drug undo that Well I was in graduate school studying chronic disease epidemiology and this was a very compatible way of thinking. If you take diseases like hypertension, rheumatoid arthritis or cardiovascular disease, they are caused by many things, they are all biological but by changing the environment you can have a great impact on the course of the disorder if not its onset - for example weight reduction may cure hypertension. I was trained to think about depression that way.

When Gerry asked me to design a psychotherapy, I was the perfect person to do it because I was uninformed and curious. If he had chosen somebody who was knowledgeable, then he might have had trouble because they would have had older psychodynamic concepts and

he would have had to fight with them. I tried to think through what made sense regardless of theory. It was totally common sense and data driven based on our emerging data on life events, social impairment and depression. I had seen some cases of depression. But I did not feel any need to take on giants or make a need or a reputation. It was very much against the times but I wasn't part of those times in the sense that I was not a psychiatrist.

What influence if any did Michael Shepherd have on all this. He apparently met Gerry as early as 1960 when planning the MRC trial and he was also into psychiatric epidemiology.

Well the UK led in psychiatric epidemiology. In America we didn't think you could make diagnoses in the community. The closest thing we had was this behavioral or psychosocial epidemiology. The leaders in the field were all English. There was John Wing who developed the Present State Examination, Norman Kreitman in Edinburgh and Michael Shepherd. These were giants in the field.

Have you ever felt that the ECA studies made the market for the pharmaceutical industry. You showed how common depression was in the community and how common conditions like OCD and panic disorder were and the industry could use the ECA data wonderfully to sell their compounds.

That was not the intent. I think this study helped everybody. It made psychiatry more rational, it helped the planning of services. It helped the pharmaceutical industry - well sure they're part of the world as well. I don't think it helped them more. It helped nosology and provided and understanding of rates, age of onset and risks. Before that cardiovascular disease had an epidemiologic base but psychiatry didn't. I'm sure that some of what came out will be revised but it changed the way we think of disorders. One of the major changes was the recognition that most of these disorders begin very early - they are not disorders that begin in the menopause or the elderly. They may occur then but they begin young. So it focussed attention on the field of child psychiatry.

Should we be treating children when they begin to get depressed first with antidepressants or IPT.

Well there are no strong data. Children and adolescents have been excluded from clinical trials. Drug companies haven't wanted to get involved because the wisdom was that these disorders didn't occur in childhood. Kim Puig-Antich at Columbia then was one of the superstars here. He was out of the loop. He came over here from Spain and began studying children in the 1970s. He developed the Kiddy-SADS (K-SADS) and he did biological, neuroendocrine, sleep, family and longitudinal studies and his question was is depression in children and adolescents the same as in adults. When he left Columbia in the 80s and I arrived, he said to me you can have my kids if you can find them. I have been following his children and we now have 75% of them - over 300 of them - Depressed Children now grown up. At present the data confirm that depression does occur in children and that it is impairing. We also know who is at risk - the children of depressed parents are at high risk - its a 3-fold increased risk. What do you do with them? The FDA has recently required studies to be done if a drug is going to be used in a population. Because of this treatment studies will increase in younger samples. The data we have for psychotherapy in children is patchy. David Brent had a study using cognitive therapy and Peter Lewinsohn has done a study of group therapy in depressed adolescents and Laura Mufson in my group has been studying IPT in depressed adolescents and there are a few other studies ongoing. That's your database, the rest is all impressions. It would be nice to have an acceleration of studies in this area.

The whole childhood area seems to bring out the psychiatric ideologies that Gerry mentioned in his 69 article. In the childhood area there is the feeling that psychotherapy is ethically the only proper thing to be doing

I think that's changing. Its certainly changed with hyperactivity. We also know there is early onset bipolar disorder. I think it will change if the studies being done now on children and adolescents are positive. If they are not positive, it shouldn't change. If they aren't positive, the question then is do these drugs not work in children and adolescents because they aren't really depressed. Our data suggest that prepubertal onset depression may be different to postpubertal onset depression but we'll have to wait for the answers. Another question is do these drugs not work because you have to have a certain maturation before they can be effective. We don't have the answers but if you want to do preventive interventions it should be done with younger populations - by the time you get to someone in their 30s who've had 3 or 4 episodes of depression you're dealing with someone who has a lot of co-morbidity and social morbidity which you might have prevented if they had been treated earlier. You don't know but these are good questions and this would be a very responsible way to spend research money. Gerry in fact pointed out the early age of onset of depression way before it became fashionable to study it.

A number of people have referred to the fact that Gerry kept on chasing ideas even when he was in a wheelchair and on dialysis

He was incredible. He traveled on dialysis all over the world. I could write the Michelin guide to dialysis units - Greece, Tokyo, Switzerland, Germany, England, Italy three times. His secretary Marlene Carlson helped to set up the dialysis when he was going to a meeting. It was high anxiety because you didn't know if they would speak English or if the records had arrived. This was his life and if he had to give it up it would have been the end, so you just did it. He worked up to the day he died because he really loved what he was doing. His colleagues all over the world helped him when he traveled, Bob Hirschfeld, Marty Keller, Jan Fawcett and Sir Martin Roth in England.

Mention of Martin Roth reminds me that he had a phobic-anxiety depersonalisation concept before panic disorder which was very much the same thing as panic disorder - did he ever feel trumped by the fact that in one sense he just didn't market his concept as well?

I don't know what he felt. He was ahead of his time. He participated in many of the subsequent international meetings on panic. When Don presented the idea at the APPA, the field was more developed, there were epidemiologic data coming out, there were more treatments.

Anything to do with the fact that panic disorder was just a more catchy term? That's true but the time wasn't ready for it. There wasn't much you could do about it. By the time Don talked about it, you could try it out in different flavours - epidemiology, family studies and the technologies were there to decide what was right or not. In the 60s the technologies hadn't evolved.

But Gerry was amazing the way he kept on working. Dialysis is pretty rough. It doesn't allow you much quality of life. Its not much quality, its just life, especially if you have diabetes as well. He wrote the letter responding to Isaac Marks the day before he died. The year after he died he had something like 3 books and 7 papers come out. He's been publishing up until this year. These are papers he was working on with younger colleagues that they have been finishing up. I showed one of them, Mark Olfson, the first draft of this piece and he commented that the manuscript didn't capture Gerry's sense of humor, that working with Gerry was fun. He had an appreciation of the absurdity in most disputes and a great enjoyment of life. Young people particularly like to work with him because he would listen to their ideas and could pick out what was important. I think 1997 will be the end of his publications. Bob Michels kidded me that Gerry was the most published author at Cornell two years after he died. I spent three years after he died at memorials and awards for him.

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