JOEL ELKES

Where were you born?

I was born in Konigsberg which is just across the border from Lithuania. My father was a prominent physician and he was first placed in Konigsberg where he had trained as a medical student. Then the War came and we moved around because my father was an officer in the Russian Army, a physician, a Jew who became very prominent in the Holocaust later. But we moved back and forth in Russia and finally settled in his country of birth, Lithuania, 70 miles from he was born in a little town called Kaunas and became very rapidly a prominent physician in Lithuania. I was educated in Kaunas, which was Kovno in those days. I had my first school training in a school which was totally original. It was a Hebrew school where every subject was taught in Hebrew and that was back in the 1925/26/27, so I read Voltaire and Goethe in Hebrew first. That was done by a band of extraordinary young people who were determined to create a school where one could get a superb general education, which to this day I treasure, in modern Hebrew, the terms being created as we went along. In fact, since we are dwelling on the subject, I remember leaning my trigonometry from stencil sheets which the teachers wrote during the summer, because there were no textbooks and so we had to learn in this way.

That was my first education and I finished there in 1930. Then my father sent me to Germany, across the border in Konigsberg. I finished school there very rapidly - I had to cram like hell because it was really becoming a Nazi school , very unpleasant already. Then I went to Switzerland and studied physics. Because my first passion, as you have seen in my autobiographical essay was physics. I did physics in Lausanne and then I came back and my father and I discussed what to do and he said well lets see what's a good safe subject , why don't you think of medicine. I was always interested, not just in medicine but in general biology, cell biology, in particular, membrane biology - I had begun to read on it already - and then my father, through his contact with the British ambassador sent me to England.

There one dark October evening in 1931 I arrived from Lithuania in England, into a totally strange country because my culture was mainly European, German. Now I was in England and I hardly knew the language really. I was accepted for St Mary's Hospital, London, where I began to study medicine. I studied medicine there. I had to support my sister as well by tutoring and so on and so it took me a long time to qualify. But I had a magnificent teachers - Alexander Fleming, taught me bacteriology . I had Sir Albert Wright - the discoverer of typhus vaccine and the model for Bernard Shaw in The Doctor's Dilemma teaching immunology and I had Charles Wilson, later Lord Mollen, Churchill's physician, teaching medicine. So I had tremendous models and also another model, who later became my father in law from my first marriage, Alec Bourne, the great gynaecologist, who started the whole abortion reform movement, by aborting deliberately a girl had been raped and then tried at the Old Bailey. And then at the same time I was an apprenticed to my mentor, tutor and beloved friend, Alistair Fraser, who was the a Reader in Physiology. He was later invited to found a Department of Pharmacology in Birmingham and I went with him to Birmingham, as a pharmacologist.

I was then already deeply interested in membrane structure, macromolecular, interaction, stereochemical fit. I was much more attracted interestingly enough to

immunology at the time than to psychiatry because I had a visual way of functioning. When I saw these molecules...

The antibody-antigen locking fit..?
Yes. I had started reading avidly Paul Ehrlich's early papers and then went on from there. Since I had no training in physical chemistry and medicine, is a very poor preparation for chemistry, I was fortunate enough to be an apprenticed for one glorious summer in Cambridge in the Department of Colloid Science, where Eric Rideal was the Director. There I spent a glorious summer studying lipid-protein interactions and spreading monomolecular filaments on the Langmuir trough and measuring Zeta potentials.

I got recruited into research by Alistair Fraser. He was the nephew of the great anatomist Fraser, who had taught anatomy in St Mary's. He was a very fine physiologist. His field was fat absorption and he had a theory about the way in which the fat in the gut was emulsified and then absorbed in particulate form, to form the chylomicrons which appear in great amounts in the blood after a fatty meal. He became very interested, I suppose, in my pre-occupation with membranes, with coating, how does a particle like this survive and he asked me to begin a study the surfac coating of these, which must be lipo-protein because it's an emulsion that floats around in the plasma. I invented a small micro-electrophoretic cell, which was published in the Journal of Physiology when I was still a medical student which had 2 gold leaf plates on side and then you watched the migration of the particle under a dark ground illumination. When we changed the pH, you could show quite clearly that the migration was charge dependant. Then began the story of what does this coating consist of and we began to study the interaction between lipids and proteins and the formation of the lipo-protein coating of a membrane and to develop certain models.

So that's what sent me to Cambridge to study the whole idea of lipo-protein layers. In the Langmuir trough, you spread a polar lipid detergent and then you inject protein underneath and as the protein crowds into the membrane it displaces the membrane and you get a measurable shift in the pressure exerted and you also get a change in the Zeta potential. I had no training in all this but I had a tremendous interest and visual pre-occupation and passion with this and Rideal was a wonderful Director and he left them very much alone. With him was also a great physical chemist by the name of Alexander Schulman, who became very prominent in this field. We published a paper in the Proceedings for the Royal Society, my first paper, when I was not yet through medical school. So I had the rare distinction of publishing 2 papers, as a medical student, which had less to do with my talent but everything to do the length which I took to qualify in medical school - because I had to look after my sister and tutor at the same time. And that really made me very interested in the whole area of physical ...

The chemistry of nerve cells... When did you become aware of the work of Francis Schmidt ?
Frank Schmidt, I became aware of in in 1942/43, when I came to Birmingham. I became interested in it because I suddenly realised that the nervous system was full of lipo-proteins. I was working on the lipo-protein of a membrane of a particle but the nervous system was full of proteins, called myelin, which was like the layers of a leek

- 70 or 80 layers - which had a density and a structure. Then I came across these extraordinary papers by Frank Schmidt where he had these beautiful little diagrams of hypothetical structures of dried myelin which he had submitted to X-ray diffraction. I asked myself if it was possible to get pictures of living myelin - is it feasible?

Birmingham in those days was a tremendous University. I don't know if it's been fully recognised the tremendous contribution it made to the War effort. Randall was working there on Radar. Pyles, the great Pyles, who was also the mentor of Fuchs, the traitor was working on uranium and writing the equations, which made possible the concentration of uranium. Moon was the professor of physics. Solly Zuckerman was Lindeman's number one assistant and therefore had access to the whole war establishment. Medawar was Professor of Zoology there; he had just done his great genetic work in rats. Hogman was professor of applied mathematics. There was an extraordinary array of people around.

There I was working away on these lipo-proteins when I had the great good fortune, as I have said elsewhere, to have Brian Finean walk into my room. It happened because I went to see the physics people and asked have you got a student who would do work on this. They said well it's not likely that you'll get anywhere because this is soft tissue and you can't X-ray this. I said well look these are the diagrams of the dry nerve, can we get them ? Finean came in and in his typical way just said "we'll give it a try". So in between singing his Gregorian chants, which he was singing at the time, he developed this cell which I also shown in lectures, which involved irrigating a tiny segment, 3 mm, of frog sciatic nerve and shooting an x-ray beam through vertically and then altering the environment of that, through drying, through alcohol, through heating and so on and seeing if the x-ray diffraction picture. This was, as far as I know, the first x-ray diffraction diagram of a living nerve . It showed quite clearly the crystal structure which was very ordered fell apart at certain stages of drying, when the water holding the colloids in place was removed.

So these things really were very exciting but I was very far away from psychiatry, except that I should say that my father was an exceptional physician and his passion was really psychological medicine. Little was know about it at the time but he talked about it and he was a tremendous person with patients, rapport and empathy and so on. So I always had a deep interest in psychiatry but I didn't know how to get into it because there was so little science around and I did want to do science. There was no neurochemistry. Page's book came later on.

So, what I am saying is that we started from this x-ray diffraction and we got onto the structure of myelin. Now I remember Finean and I had with our hearts in our mouth going to see J D Bernal, who had written the Social Function of Science, and Alan Hodgkin. Bernal looked at these films and said "that's very interesting, that's possible, go on, go on, just go on, this is worth doing". Rideal by that time had become the Director of the Royal Institution so we had at our disposal the great x-ray tubes which Lawrence Bergin had used for his famous crystallography studies, but we had to cool the tube because we had a long exposure. I remember standing on a ladder putting ice around the tube to cool it sufficiently for the 15 minutes which we would need for exposure without the thing blowing. We got very good photographs, which we took to Alan Hodgkin. Hodgkin had not yet written his 3 great papers on nervous conduction - they were still in manuscript form or in press, I don't remember

but they hadn't come out. I remember that he was sitting there with a thermos and a sandwich looking at these pictures and he said "they're interesting, you should go on with this".

And of course that was all we needed. Just a little encouragement. Because we were totally alien corn. We were neither in medicine, we were not physical chemists, we just didn't belong anywhere but we went on doing this. That was when I became really interested in the chemistry of the nervous system and started reading avidly about it and about the action of drugs in the nervous system. At that time the drugs really were paraldehyde, chloral hydrate, barbiturate and then very important, it had just come out, Dilantin.

Now why was that important. You refer to it often but don't really say why it was important?
Why was it important, because from our studies which I will come to in a moment, on catatonic schizophrenic, with Charmian, my late wife, we had begun to regard schizophrenia as a state of hyper-arousal. This was a little later and then Hill and Pond had already begun to study the effects of the relationship between epilepsy and aggressive behaviour, so we just wondered whether an anti-convulsant could possibly reduce the state of arousal without impairing consciousness. But this came much later and at time the famous visit from Thrower came and we got Thorazine and began with it rather than Dilantin.

But let me just backtrack on the chemistry. You see the war had just begun. I was an alien, with a white card, curfew, the whole bit and one day two men came to see Alistair Fraser, clearly on official business. They sequestered themselves for an hour with Alistair Fraser and I was wondering was I going to be deported. I was alone, I had to support a sister, the only protector I had was Alistair Fraser. He called me in and said these gentlemen have come to do a security clearance on you and you've passed. They'd like you to work in the chemical defence experimental establishment on anti-cholinesterases, the gasses, atropine-like substances and so on.

So I began to visit Porton, as one of the team. And I began to sit in on quite important and critical meetings at which the whole question of anti-cholinesterases was discussed very thoroughly and the question of hallucinogens also came up. LSD had not yet been discovered. That came about 3 years later. We are talking now about 1943/44/45. So I began to read avidly about chemistry of the nervous system and found that there was damn all there except for a few laboratories. There were 3 really. There was Derek Richter's laboratory in Cardiff. There was Quastel's who Richter had succeeded.

At this stage Quastel had gone to Canada hadn't he?
Yes. Richter succeeded him, I think. There was Weil-Malherbe whom I recruited later on and took with me to America. At one point he was in Runwell Hospital. That was a very critical step not only for him but for the field because the conversations between Julie Axelrod and Hans Weil, in our laboratory, really resulted in the sparking off of this whole story.

Who was Hans Weil-Malherbe?

Hans was a very fine neurochemist who became interested in the nervous system a long time ago. He worked particularly on amine metabolism as well as glucose metabolism, on glutamine metabolism. An extraordinary gifted but extraordinary shy, retiring, self-effacing man, with the gentlest smile, a gentle, gentle person. Not appreciated at all but mighty in his writings and that's what attracted me to him.

He came from Germany?
He came from Germany before the war. He was a Jewish refugee. So that was that. Quastel, already I knew, Richter I knew, Weil-Malherbe I knew and then there were the Maudsley people who were beginning to start but they came in later. McIlwain came later with his slicer. These were the pioneers, working in mental hospital settings. And there was Crichton-Royal Hospital in Dumfries with Mayer-Gross, whom I recruited to Birmingham later on as Clinical Director. And that was about all in Britain. Then there were some labs in France. In the Universities there was nothing on the chemistry of the nervous system - it was really a who-would-mess-with-that kind of attitude. We, in Birmingham, were the first university to begin this work and to take the subject seriously. I cannot state the importance of that, the risk which the University took, the step which it took in backing us, me, Bradley and others in this very strange amorphous field.

So why did the University take the step. Was it that the authorities were particularly enlightened or were you particularly persuasive, or was it some combination of both?
It was a combination of the two. You see I earned my spurs in science. I was regarded as a reasonably good scientist. The x-ray diffraction studies were original, somebody said deeply original. When we started to study the anti-cholinesterases, I said well lets map the cholinesterases of the brain and we started to do this sitting in a cold room, gloves on, dissecting rat brain carefully into 40 or 50 slices. In those days there was no Beckman's spectrometer. In those days when we were investigating cholinesterase you had to take a piece of brain, homogenise it carefully, then elute the fluid, put in choline and acetic acid, measure the synthesis and then assay the amount of acetyl-choline using guinea pig ileum. Can you imagine the labour of that 5-step technique. It took 2 technicians or 2 PhD students to map a tiny area of the brain. We did that very carefully and that it what impressed people - that this is a serious person who is doing some decent science and the work was accepted in the usual journals. Quote-unquote, he's not just a psychiatrist or not a psychoanalyst. I could always defend the science. So that began in the neurochemical laboratory

You looked like you were going on to say that while you earned your spurs in science, your role has been to come up with ideas...
Yes, very much so. I gave a guest lecture a year ago at Vanderbillt and they took a recording of me there for ACNP because I was the first President and Fridolin Sulser, who is the Professor of Neuropharmacology there, asked me this very question and I said my role has been really that of a gardener. A green-house builder and I had, I suppose, the skill of spotting very talented people and making damn sure that they got what they needed.

I already saw a new field coming. With the anticholinesterases, precision tools 10^{-5}, 10^{-6}, 10^{-7} molar, my God, I said that is precision pharmacology, so there's a future for this

no matter what. I also began to see dimy the outline, which was my central contribution to the science of the field, which I will come back to, of the whole principle of regional neurochemistry. I invented the term and used it for the first time with Seymour Kety in the Third Neurochemistry symposium, when we were sitting around and I said lets call this symposium Regional Neurochemistry. The idea of regional and uneven distribution of signal molecules in the brain was converted into my Ciba paper which goes into the idea of regional neurotransmitters and receptors in the brain. This came really in 1951/52/53.

Let me ask you about that because that's clear from some of your contributions to meetings that were put together by Derek Richter and others but in the UK at the time you were mixing it with a group of people like Dale and Feldberg and Marthe Voght, who while they were into acetylcholine, they didn't concede that it was involved in the central nervous system. And as late as 1960, Arvid Carlsson was saying that he came to a meeting in the Ciba Foundation and while they had all the evidence on the drugs and he was able to show depletions of neurotransmitters etc etc, Dale and Gaddum and all of the other big names did not accept what was happening.

I know. I can imagine what he was up against.

Why should this have been the case? Was it because the power of the neurophysiological paradigm was so dominant, ..
Absolutely. I was given advice by Henry Dale, who liked me very much. He wrote me personal letters from his retreat in the Lizard in Lands End. He said to me Elkes, for Gods sake you're a good pharmacologist, work on the heart, work on the gut, stay out of the nervous system, it's a sticky mess, you will come to a sticky end. This was actually said to me. I am jumping around but when Philip Bradley and I demonstrated for the first time our conscious cats at the Physiological Society, we had one asleep in the ?? chamber, with the leads sticking out and Burns came up and said "oh very interesting, very interesting, what anesthetic are you using?". I said, "Dr Burns, there's no anaesthetic". "What do you mean there's no anaesthetic, there's a whole bunch of wires coming out of this cat". I said "no, there's no anaesthetic" and I just clicked my fingers and the cat stood up and the EEG changed of course straight away to an alert state. Burns said in his typical accent, "my word, my word, goodness, that's really something, that's really something". And that was the first time that they conceded that this could be done .

On the chemical front, Feldberg saw it straight away. Why? Because he had worked with Sherwood with the intra-ventricular cannulas and he saw the central effects of acetyl-choline. In that classic paper, which I quote again and again which has not received sufficient attention, by Feldberg and Vogt, in 1948 - after we had started in 42/43/44 - they had shown that there are areas which get on without acetyl-choline. They showed this nice thing, in the retina, where one layer used acetyl-choline and another one didn't and that both projected separately to the geniculate. That fitted, David, with my vision of regional, uneven distribution of cell populations which had slightly different enzyme constitutions, which would grow into certain areas and populate and colonise the cortex while other members of that group would populating other areas and so on. In fact, I developed a whole theory of schizophrenia around that.

Can I put it to you that perhaps the reason you were able to see this was with along with people like Brodie and Axelrod you weren't a physiologist. It was because you hadn't been trained in that that it became feasible to see what the physiologists couldn't see.
Yes. Brodie and Axelrod came later, as you know. Brodie was fired up by a Macy Symposium at which he and I spoke together - he became a tremendous pal of mine. But exactly, we were outside the pale. Look I was outside the pale in physical chemistry, I was an alien. I was a medical fellow doing x-ray diffraction. I jumped around a great deal. Why ? - because this was how my mind works. But I had a very clear precise vision of this principle of regional processes in the brain, of regionally organised neuro-regulatory substances. Hess, tropho-tropic/ergo-tropic came into the picture some...

When did he come out with that idea?
I have forgotten now. It was fairly early on. His star pupil in England was of course Geoffrey Harris; we were medical students together and he became father of neuro-endocrinology of course. But this whole idea of regional distribution, and I talked of chemical fields and of high and low titres in the brain stem very early on - I was pleased about it, people kept on saying well how's your titre today and how is it in the morning and the afternoon. And I said well I think , if you know how to look for it you will find it is different. So I had this principle of regional organisation of the brain, regional economy in the brain, of the operation of chemical fields in the brain and so on which I formulated first in the discussion of the paper by Bradley and Elkes in Brain. I wrote the discussion and Philip still remembers saying we have no evidence for that and so on and I said "Philip we have got to put it down if, this is how we are going to do it". He called me up 30 years later and said "Joel you know of course this paper is now a classic". And I said to him, across the Atlantic, Philip we didn't really know what we were in to. And in his typical wonderful manner, with a chuckle, he said "Joel it's just as well because it would have made us impossibly arrogant if we had known what we were formulating ". This was before Chlorpromazine. It was creating a theoretical basis for the advent of the psycho-active drugs.

Was this before Chlorpromazine?
Well, Chlorpromazine came in in 1954, but Philip's doctoral work was done in 48/49/50/51. The chlorpromazine story came in later, we were still on the anti-convulsants then. But the vision, literally the vision because as I say I am a visual animal was there in 1950/51/52 - the idea of a family of neuroregulatory compounds was there in 1950/51/52. The first formulation of it was in the Journal of Physiology in the abstracts. Feldberg was very interested and..

Who was Feldberg? What was his background?
Feldberg is, I think, still alive. He must be over 90 now. He is a German refugee from the Kaiser-Wilhelm Institute who came under Dale's wing and became Dale's star pupil. Marthe Vogt was Feldberg's collaborator and she did the dissection of the columns of choline acetylase in the brain.

And she came from where?
She came also from Berlin. She was the daughter of the great Herman Vogt, the pathologist. I don't know if she's alive still. But I felt that there is, as I have said in these early papers, a connection between the peripheral and central nervous system, that

there is a chemical central re-presentation, the autonomic nervous system, and that the same families of compounds have undergone evolutionary twists and changes and have been adapted for various purposes and the same kinds of cells exist in the brain as in the periphery and that is why in one paper
I asked a fellow in the Department, by the name of Ginser, to look at the effect of psychotropic drugs on the gut and I predicted there would be effects. And there was. And then of course Paton, WDM Paton, made his reputation by studying the effect of opiate on the gut. Not on the brain but on the gut. So, I saw this connection between the autonomic nervous system and the central representation which is built into the circadian rhythms and all that.

So we began to map the brain. Archibald Todrick, who you know, is now retired, became our colleague in neurochemistry and then of course Philip walked into my lab from Grey Walter. He had been in Bristol and he was an insect physiologist and he had done a micro-electrode study on cockroaches. I said can you do something on a cat and he said "well I'll try" . That was his PhD thesis and he worked up this magnificent technique, which was really a stunner because there was no penicillin in those days. We had some sulphonamide and we had to apply suphonamide powder every day and nurse these cats, as if they were in an aseptic environment, until the torn skin healed and so on. Then once we had them they were powerful and we were working into the night. Every week we had new results and we had to build a theory as we went along. My theory was the theory, which I have outlined, which was that the brain stem is different from the cortex and there are different cell populations in different enzyme systems and we predicted certain effects. Then Moruzzi and Magoun came out with the idea of the arousal system and I said to Philip well lets go after that one. He had read ??? and the encephale isolee, which was done ten years before Morruzzi and Magoun had done their arousal system and sure enough we found that there were sharp difference between the effects of an anti-cholinesterase on the encephale isolee.

Then we got one of the very first samples of LSD from Sandoz. This must have been in 1949 because we did our first experiment in Christmas 1950. That was when my contact with Rothlin was established. We tested it in the cats and we found then that these effects were dependent on afferent collaterals, on afferent input. So I postulated, in the discussion in this paper, that somehow LSD acts on the receptor which is activated by an indole, which plays a part in an inhibitory role in structuring sensory information. If for sensory information you substitute sequential thought, you have the whole idea. This pattern of inhibition, which is in some way disorganised by LSD. Aghajanian, of course, came up much later confirming that completely. So to come back to what was..

This helps explain why you saw things this way and something else which is that in the Tanner volume, where it is clear that Eccles that Dale and people were beginning to consider the prospect that acetyl choline might be involved in the central nervous system but at this stage you had moved on to, of course it's involved but there are other things as well, which is so funny in that they were just beginning to get around to it but acetyl-choline is not all that important anyway, there are other things.

Yes, that is correct, that is correct.

What happened then was that we had the chemistry which came from the work of myelin and the anticholinesterases, we had the electro-physiology and then we moved to human behaviour and this is where Charmian became an important figure. She was in general practice. We were very poor. I lived on a tiny Stewart Fellowship. We were talking about psychiatry and I had just been to listen to Jean Delay, soon after the War, this must have been 1947. Jean Delay came over to talk about his work on stupor. And he mentioned the work on amphetamine.

Amphetamine shock was something that he was in to.
Yes exactly. I began to read about catatonic stupor and I became tremendously impressed by the psychosomatic implications of it. This was a state which includes the voluntary system with rigidity, it includes the autonomic system with acro-cyanosis, mutism and so on. I was not aware of the work of Lindemeyer which showed that amytal could bring people out of a stupor. So we started with amytal and Charmian gave 300 mg intravenously in the old-fashioned syringes, there were no drips, nothing like that. Steel needles, glass syringe and you got the vein and we noticed straight away the amazing the awakening effect - it was really like that film, Awakening, these people came out of the stupor, they would talk for 40 minutes, they would associate, they would remember what flower you had worn in the button hole on the Sunday, we noticed also some pinking of the extremities, it was like an Anderson fairytale, but then they would relapse into stupor. This was on just 300 mg which seemed reasonably small. So Charmian and I discussed this and said lets do an experiment and what we did was to find 18 catatonic schizophrenics ..

Where has catatonic schizophrenia gone. We don't have it any more.
No. It was essentially a product of over-medication but probably mainly neglect in the management that went on in mental hospitals then. So we found 27 good catatonic schizophrenias. We went to the superintendent, a man who again is a marvellous person in my personal history, J J O'Reilly, who was the Director of the Winston Green mental hospital. A nice Irish accent and he said "yes, we'll set a room aside for you". We got a little room and we set up a thermo-couple arrangement to measure hands and feet temperature. We set a steriliser to get the injection and also Charmian and I thought up a way of measuring muscle tone. We had a sling with a weight going over a bicycle hub, pulling down the number of kilograms which it would take to move from full flexion to semi-extension, which in stupor was about 5/6 kilos. Then of course, photographs. And Charmian had the idea of letting them to draw at the same time as they came out and so you would give them a piece of paper, pencils, coloured pencils and prompt them and they would just scribble. We had 18 patients over a year and some 110 experiments. We gave amytal, amphetamine, mephenesin, which had just come out as an anaesthetic.

We gave these 3 drugs in random order and found quite a consistent effects. With amytal there was a marked psychomotor effect, a marked drawing response, talking and so on, flushing of the cheeks, a rise in foot temperate. With amphetamine, which would send me roaring and wailing, there was a deep stupor, rigidity, blood pressure rising which was quite alarming at times, and total mutism. With mephenesin, there was very nice relaxation of muscle, no effect on the face, no effect on the temperature, no effect on the drawing response and no effect on verbal behaviour. So immediately I said "my God this is selective, this is a selective effect on a schizophrenic syndrome". This was before Thorazine. So we were off and it was at that time that I said that

schizophrenia and stupor is a state of hyper-arousal, an inhibitory filtering process which does not work, which is chemically mediated in the brain stem. The selective effect was very impressive and at that time we were about to go off on to anticonvulsants when in walked into my office WR Thrower, the medical director of May & Baker.

We had a conversation which I still recall vividly to this day. He came in very properly dressed and very proper generally and said can I see Professor Elkes and he said "Professor Elkes, this is not a routine visit, do you mind if I shut the door?". He shut the door, and then he pulled out of his brief case, which he unlocked very carefully, a manuscript by Delay and Deniker. He said "we have just got this from France, would you please read it". I read it. This was the first paper by Delay and Deniker. And I said "quite honestly this is too good to be to true" and he said "well that's why I'm here, because we've just got the rights from Rhone Poulenc, for compound RP 4520 and we have 500 gms in the safe. We'll make up the dummy and real tablets, will you conduct a controlled trial?". I go home to Charmian and say "honey we've got another little job on our hands". She said yes let's do it in her quiet way. She died a year ago.

We did it. She set up the trial, moving into a mental hospital, in those days, with a clinical trial, no instruments, no calibration tools, nothing. She assembled the staff on the ward, she selected 27 patients. I said err on the heavy side, smearing faeces, screaming, the noisier and the more over-active the better. So she selected 27 patients. We explained to the staff what we wanted to do. We had to give them instruments for recording day and night. We tested the instruments by recording what the words meant to the different staff, asleep, fully asleep, half-awake, awake, over-active, screaming and so on and constructed this scale. Then we designed the trial as a blind control trial, 6 weeks off, 6 weeks on, 6 weeks off etc., with a dose of 250mg on average for the 42 weeks. When that trial came to an end, I can still remember the occasion. I was in the room where it happened recently and I have a photograph of the room where we sat around the oak table, when I gave the lecture when they inaugurated the new Queen Elizabeth Hospital, in Birmingham.

Anyway, I was invited to be there at the ceremony in the hospital and they took me to Winston Green Hospital and I sat around that same table, the same oak table where Charmian had spread all the documents and then we started to read out the scores of the ratings and then match them against the codes. We started putting them on the blackboard and within 10 minutes we had seen something which we had never seen before - the scores were different. In 7 patients the scores were just astonishingly different, on-off, on-off. She had also observed all the side effects, the memory, the pigmentation and other things , which were later observed in subsequent trials, despite the small dose - 250 mg.

I remember talking to Sargant about it. We were trying a new drug, I said, and he said it will turn out like another barbiturate. And I said no, I don't think it will quite. Then there appeared a paper and an editorial which Sargant wrote in the BMJ, the 1954 paper which mentioned this as a novel trial, or something like that, which I suppose it was. It was a first controlled trial of a psycho-active drug. ***

Were you aware of any of the other trials that were happening at the same time? Schou did something very similar. Double blind placebo control with a cross

over design with Lithium, which started in 1952 and published in 1954 and Linford Rees had done some trials with cortisone in 1951/52 but they hadn't shown that it worked. He did he Chlorpromazine trial in 54 and it was published in 1955 and Michael Shepherd had begun a trial on reserpine in 1953 but that didn't get published until 55.
No I was not aware of those trials.

It seems that a few people came to the idea of this control design around the same time. Its curious how these things happen.
Yes, which is a good thing. It was a coincidence. But as far as we know, we acted independently. There were the Delay studies and Lehman came a little later, if I remember rightly and Kline with reserpine.

Yes but these were just open trials.
No they weren't but as far as we knew we were inventing it. And my beloved Charmaine did it magnificently.

Why did you invent it, were there any other influences? The idea of a placebo had been around with Harry Gold and the double blind idea was also there, but putting it all together, what influenced you? Had you been influenced by the 1948 streptomycin trial?
No, David I knew nothing about of the conduct of trials. The only person I spoke to about it was Lance Hogman and if I remember rightly Myre Sim who was in Birmingham at that time. I had spoken to him and, if I remember rightly, he had published a trial or two and either Myre Sim or Lance Hogman and talked about the blind self-control design I think. I forget whether I mentioned it in the paper but it was again an obvious idea but we had this feeling David, that there was nobody to go to, there was nobody to talk to. Aubrey Lewis of course, you could talk to him and he was very encouraging. Michael Shepher had not yet become the shining lnight that he was later to become. The others were busy with their own things.

What emerged, gradually from this programme which was called Drugs and the Mind, was the concept of a Department of Experimental Psychiatry, which formalised itself in discussion with Charmian, in discussion with Heinrich Waelch and others. Actually, I should backtrack a little perhaps and tell you that by that time neurochemistry was beginning to take off and my contacts began with Heinrich Waelch, with Jordi Folch at Harvard, who had started up the Rockefeller Laboratory of Neurochemistry, with Ruth Flexner ??, but mainly with Heinrich Waelch of Columbia who was the dean of neurochemistry and we developed this idea of a symposium to put the idea of the chemistry of the nervous system on the map in the modern way. I talked to him at that time about this symposium of which I became its chief agent, the organising secretary - it was a magnificent symposium - but also about the concept of laboratories and a clinic all under one umbrella and free conversation and opening up a completely new field. I felt in a strange way, that I had been given a task. I never had any missionary zeal about it or a feeling that I'm sent to do that, no but it was much more a tremendous, joyous playing with ideas and executing ideas and bringing it all back to psychiatry and to physicianship.

Can I ask you about that because what you've elaborated there is a different vision to the Francis Schmidt vision. Schmidt is often credited these days as

being the founder of the idea of neuroscience and it seems to me that yes he had a key role but in a very non-clinical neuroscience. You began in very much the same areas as he did but seem to have moved in a very different direction.
Yes because I was much more interested in function. I was deeply influenced by Sherrington and his seminal volume on reflex action and the nervous system and I am very much a people's person. I always felt that if we are to help people we must work in context. We must provide an environment where there is work in context, there is continuous conversation, and that is how the idea of the Department of Experimental Psychiatry arose, which was a very fundamental shift. For me one of the big moments in my life was when the Dean of the Medical School then Sir Leonard Parson's who was a fine geriatrician called me in and he said, "you're working on these drugs and mental illness, is there anything to it? ". I said "yes Sir Leonard, yes I think there is I think it is very important". This was before Chlorpromazine. And he scratched his bald head and he said "well Elkes why don't we send you to America for a year. If you find a Fellowship I will give you a year off and you'll learn some psychiatry - you can learn it all in one year, can't you?". That was the attitude. I said I would love to go to America and I got a Fullbright Fellowship and then a SmithKline and French Fellowship.

Why did SmithKline and French give a fellowship because this was before they got involved with Chlorpromazine or anything to do with psychiatry.
Yes but they gave me a Fellowship in 1950/51 to go there. They visited me and they thought there was a future. And then also, don't forget, that SmithKline and French made an awful lot of money with Dexamyl. So they had slipped around in this area before Chlorpromazine. They gave me a Fellowship, a bursary and when I got a Fullbright Fellowship, I went to Bellevue first and then to Yale and then to Norwich State Hospital, where the found that they couldn't employ me because I was an alien, so they gave me the lowest assignation, namely an intern. So on the roster by the Superintendent's officer there was this a list of about 20 of them and then intern, one J Elkes. Then one day, David, I get a telegram from the University of Birmingham, the Senate this day has recommended the creation of a Department of Experimental Psychiatry and invites you to accept the Directorship in the Department of Experimental Psychiatry, Birmingham. I went to the Superintendent and I said "look, Dr Kettle, I've got this telegram and he just couldn't believe it". He said "my God, that's a promotion from intern..."

So I went back to Head up this new Department. I didn't really know the shape of it but I knew that it had to have a strong clinical arm as well. And it's there that J J O'Reilly again, in combination with the Dean, at that time Sir Arthur Thompson, came up with the idea of using this old Cadbury mansion, which was a place for burnt out schizophrenics... why don't we empty it and put Elkes in there and give him this clinic. Over the year systematically it was emptied and the Uffculme Clinic was created in 1952/53 as a result of that. Harrington, who Mayer Gross recommended to me and who I put in charge, became Director of that. It had 44 beds, a Day Hospital, an outpatient department, a patient club, because I was very strong on social support and of course it was a magnificent setting for symposia and so on. We had many symposia there. Tinbergen spoke there for the first time to a psychiatric audience. Michael Chance, the ethologist, I gave him a lab in the Carriage House so that he could carry on his work on crowding and amphetamine. Suddenly we had an extraordinary range from fundamental neurochemistry, physical chemistry, through enzymology, to electrical activity in the brain, to fellows working in schizophrenia, to an outpatient clinic

where you could carry out controlled trials, to social support systems, day hospitals which was very new in those days - Bierer had just done it and we adopted it straight away. Suddenly there was this Department of Experimental Psychiatry which was really a Department of Psychiatry with a difference. It had labs but labs in context.

The same principle applied when I was invited to the NIH. They first came after me in 1955. Kety and Cohen. Cohen was Director of the intra-mural and Kety was Director of intra-mural research and he said "we'd like you to come over and see what we can offer you". I came over from Birmingham to Building 10 on the NIH campus and they took to the 3rd floor and they said, "this is your space". One floor of Building 10. I met Axelrod, Evarts, Butler, the gerontologist, Shakow was next door, McLean was next door. They had decided to call it the Clinical Neuropharmacology Research Centre. But by that time the Medical Research Council in Britain had been very good to me. The Rockefeller Foundation had been so good to me, they had given me a lot of money - one of their largest grants in Europe, the man who came over, said to me "well we are investing in you because we think this could be another centre like Penfield's center in Montreal. We invested in him and we're investing in you. So I said to Seymour "I can't go, I just can't go. I am an alien but my roots are in England; this is my home - this country has been very good to me". I couldn't leave; for two years I couldn't leave. Finally Seymour called me up and said "well Joel I've offered you the best job I've ever had. It is so good that I am resigning from the Directorship and I am taking it". So he became the big chief of the Laboratory of Clinical Science, this world famous which had Sokolow in it and Kety of course, and Julie Axelrod, Butler and Bryon Williams and Fritz Reidle, the paediatrician, next to the labs of Dr Shakow and Dr McLean. It was was unbelievable array of talent.

Two years later he called me up again and said "well my lab is going fine but we still want you, will you come" . So I came over and I said "well lets do it differently this time". Let's put the labs where the patients are because I want everyone of us, whether you work on micro-electrodes or neurochemistry or a behavioural trial to know what this is all in aid of. I want the scientists here, when they walk through the canteen, to see schizophrenics having a cigarette and coffee. I want it in context. The science will be very good but I want it in context. So we went to St Elizabeth's Hospital and spoke to the Superintendent there, Dr Overholsen and he gave me the whole of the Alison White building.

We made the basement into labs, with offices upstairs on the 5th floor and the rest of the building for the patients and since then, it has been hollowed out more, with more and more labs and all the work which began there is really famous now.

I brought Salmoiraghi from Montreal. I had Max Hamilton here as a first Fellow. He wrote his 10 lectures on research which became the famous lectures, while he was at St Elizabeth's. He was as rough as hell with the residents. The same principle applied, experimental psychiatry call it what you will but it's got to be in a clinical context. I think we in Birmingham were the first to lay this, to make this path of neuroscience in the context of mental illness in a coherent way rather than in a separate way. Yes we had labs, we had a hospital and we had a research department, which even in the great days of Columbia, Heinrich Waelch, who was a great neurochemst, had damn all to do with the patients. Jordi Folch was interested in particularly macro-molecules, lipoprotein but I always wanted this context maintained. I often said to Seymour

“Seymour we are still breeding teams but ultimately I’d like us to breed just a few people who have the team in their own head, the whole ball of wax - they are damn good psychiatrists and they are good neurochemists, or good neurophysiologists and so on. And that’s what we began to do in a minor way in Birmingham and developed in a much fuller way in Washington. When I came to Hopkins it was easy because then I had good departments of pharmacology , neurochemistry and so on and you could begin to cross-breed people and out of that rose Sol Snyder, Baldessarini, Mike Murphy and God knows how many. A whole array.

The same happened in St Elizabeth’s. We had Floyd Bloom who came there to his first job from Yale. He succeeded Salmoiraghi, who succeeded me and then Richard Wyeth succeeded Floyd Bloom to this day who’s married to Kay Jamieson who wrote this wonderful book on manic-depression. These were very strange zoos, David, because on the one hand you could have of the biochemical accomplishment of Sol Synder, who was a biochemist but who had an extraordinary sense as a psychiatrist and I had people like Stan Grof, who I brought out of Czechoslovakia.

Yes, Stan worked on LSD and holotherapy?
Yes and I brought him out of Czechoslovakia, gave him his first fellowship. He was, in those days, very stiff and I kept on embarrassing him when I found him standing very stiffly in the doorway when the Geheimrat passed and he’d say “please doctor, don’t embarrass me”. Stan used to bow formally when the Professor passed and that kind of thing and I had to get him out of these bad continental habits but what I am saying is that it was a strange zoo there. There was John Money on sexual behaviour, Jerome Frank, persuasion and healing, Joe Brady, a star pupil of Skinner’s, and then an array of clinicians of all kinds and there was a wonderful conversation going on every time and it was all about the interface, the thin permeable membrane, between science and clinicianship, between science and service. The condition was “please ladies and gentlemen listen to each other, go to each others seminars”. I set the tone. I was always there myself to open the discussion and looked around to see who was there and they knew if they were not around they would be asked why they were not around and that’s how it developed.

I was living in Hopkins from 1963 to 1974, living in Adolf Meyer’s room. I had Adolf Meyer’s library next to me. When you read Meyer’s work and manage to cope with his convoluted sentences, you find that his concept of psychobiology is very close to mine. Psychobiology and the continuum of molecular biology into life is the tremendous task and responsibility of modern psychiatry. Because with respect, there is no discipline in medicine which is as broad and as deep as is modern psychiatry. If it is practiced well it is molecular biology and genetics, it is clinicianship, anthropology, linguistics, the whole thing. Where do you find a science like that.

You’ve touched on a huge range of things. Can I take you back to Jean Delay. What was he like?
He was a very cultured, cultivated man. A savant in the French sense, an author. He wrote impeccable French and was a great friend of Andre Gide, I believe. A very cultivated, polite gentleman. Deniker was much more fiery. He was the active partner in the marriage. But I liked him a lot and I was on several committees with Deniker - the CINP etc.

Philip Bradley suggests that Rothlin came to Birmingham before the CINP started and that even at that stage he had an idea for CINP, which is interesting because in terms of the origins of the CINP, other people say that Rothlin at the start was against the idea of the CINP,
No. I can witness to that. He came to us for 3 days. A very unusual visit, with Mrs Rothlin. He was very impressed by what we were doing . The link was probably through LSD, although he became interested in the whole field of as you can see in his preface to the first volume of CINP. We discussed two ideas. The journal idea came, I think, from Willy Mayer-Gross and myself for a journal which became Psychopharmacologie. We had already discussed it with Deniker, Jean Delay and so on. The CINP idea was discussed with Philip and Rothlin. I don't know, as I said in my paper, whether the word Collegium was used at that time, but the idea was discussed at the time. No, Rothlin was not against the CINP. He was very much a protagonist of it. He was a very precise, reserved, formal Swiss professor.

Philip Bradley seemed to have not been very keen on him, he found him too authoritarian.
He was. There was no question of that. A difficult Swiss professor yes and in meetings he was authoritarian and committee meetings too,. In the second or third meeting there was a tremendous altercation between various delegations and, since I speak three languages, I had to intervene and so on. Yes but I think the idea of the Collegium was in his mind, just as the idea of the American College, really originated I think in fairness with Ted Rothman, who discussed the idea with me and Jonathan Cole and we said "yes by all means" and then we went and got busy.

Can I pick up on Fritz Freyhan?
He was in Delaware. He spoke beautifully and he wrote very well. He had a certain continental, elegant, refined manner and dress and a sort of slightly nice continental wit about him and he had a view of psychiatry which was akin to my own, which was reflected in the title of his Journal - Comprehensive Psychiatry.. He was totally surprised, as was Weil-Malherbe when I recruited them out of blue to come to Washington. I recruited him and I didn't know how it would go because he was not used to the ways of Washington. He was not used to civil service side of things. But he became quite ambitious, pushing and so on and I had to slow it down, but he was a strong, supporter particularly of the work on social psychiatry in relation to the effects of drugs and social re-habilitation and he wrote on that extensively. There's a paper by him, and Mayo, a black lady who worked with him at the time. But he was not very good with residents and staff. He was very continental, stand-offish. He didn't have the American way of warmth and informality and so on, so I had to compensate for this. But he was a stalwart supporter of mine and he succeded Anthony Horden, who I had briefly brought him into the picture. Hordern and Lofft, they organised some very interesting trials for us and they were also translators to the lay administration of NIH of what we were about - we conducted some very good trials, which figured in testimony to Congress and got us some money.

Fritz played a significant part in early CINP meetings. He was clearly one of the people who was thinking about the field and the implications of drug treatment for theories of psychopathology. But he died early, what from?
A heart attack. He was in his fifties I suppose. He had a second marriage, a good one I think. Nice woman. A German lady. He was Jewish, she was not. We saw a lot of

them in Washington but I can't tell you much about him except that he had a philosophical streak and he was very well read in continental literature, particularly the German literature. He read all the philosophers, like Jaspers, and used to quote them. He was very encouraging to me, personally. I will confess to an idiosyncracy. I never felt sure of myself because I have not been though the mill of clinical psychiatry. I have learned it but I haven't studied it. I had an instinct for it and I was a good diagnositician and although I say so myself, I was a good therapist, but I haven't had the formal training. So when I undertook to write a paper on schizophrenia, I turned to Fritz. Now at that time I been thinking about computers and organisation of information and so on and he wrote me back a note immediately, almost within a day, saying what an extraordinary paper this was, which gave me a real boost in continuing to think along these lines. The paper talks about the organisation of information and the concepts of regional economy in the brain and the role of amines other than norepinephrine - I mentioned dopamine at the time. I sent it to Arvid Carlsson in fact who later quoted it but perhaps didn't quite get the links between information processing and chemical organisation within the brain.

What about Willy Mayer-Gross?
What a wonderfull, wonderfull man. Willy. I knew his book which had just come out. I heard him and he heard me and we started talking. I asked him "Dr Mayer-Gross, what are you doing these days, are you retired?" and he said "oh I'm thinking of retiring", "Well would you care to consider having a quiet corner in Birmingham?". "Yes, I might think about it". Then I call him up again and said "Dr Mayer-Gross, I have the money together, will you come?", "Yes, I will come." So he and his wife came to Birmingham and it was just wonderfull to see him because he was always buoyant, optimistic, pragmatic, strong, workmanlike. He had these strong hands and every he thought of doing had a strong base to it. He was a tremendous phenomenologist. He was also a very sensitive man, insightfull into the nuances of interpersonal relationships. Not always, for example one of his bete-noires was Myre Sim and Myre Sim hated his guts and my guts because I was the usurper and he wanted to be the Professor of Psychiatry. Myre Sim was a tremendously talented man. I told him that I greatly admired his great book, tremendously talented but he also had these persona difficulties.

The other thing about Mayer-Gross was that he was an optimist and as the new young man I was overwhelmed in those days opening up a new field in a strange environment - it was like a curate's egg, people liked parts of it but My God why are you messing with this? I used to get overwhelmed by this but there used to be these wonderfull moments, when the door would open slightly to my room and first this big Hebraic nose would appear, then gleaming gold spectacles and then the whole beaming face of Willy and he would say "Don't take it serious, don't take it serious" and that gave me as a young professor tremendous strength. He helped me with Uffculme, he helped me with recruiting John Harrington from the Maudsley, he helped me with other things and with the idea of Psychopharmacologia because he spoke to Jung and Mignon and others. Then I wrote for him a major chapter for a Hanbook for Psychiatry published by Springer, which many people have asked me since why I hid this away. Historically this piece was one of the first times many of these concepts have been put together.

Willy stayed there after you left?

Yes, he died there. He was a refugee. His wife was catholic. They wanted to go back to Heidelberg where he had been and his wife's whole family was still living. He was packing when he had a massive heart attack. He's buried in Birmingham and I spent an hour looking for his grave the last time I was there and couldn't find it. He was a very special person.

Another person early on was Abe Wikler, who seems to have been very important in the early years but who has been written out of the history. What was his role?
Abe worked in the addiction center in Lexington. His work on addiction was tremendous. It showed for the first time the linking of the environment to the symptomatology of addiction and to its course - to the addiction process. He also wrote in 1957 on the relationship between Pharmacology and Psychiatry, published by Williams and Wilkins, which was a prophetic book because for the first time it put together neurophysiology, experimental psychology and psychiatry in one volume. He was also important as a critic and he became a very discriminating editor of Psychopharmacologia, where he put his own stamp on the quality of that journal. He had an eclectic vision and could critically evaluate a paper from a psychiatrist, an experimental psychologist or an electrophysiologist. His personal history I don't know.

What about the 1956 Conference on the Evaluation of Psychotropic Drugs?
I was starting to commute by that time. At that conference, Ralph Gerard who was the convener of the conference and Jonathan Cole, who was a young man, totally unknown to me, got together this meeting. By this time we had had the Macy Symposia, the Neurochemistry Symposia, which were tremendous meetings - we were building the footings of a new science, neurochemistry, electrophysiology, animal behavior and clinical trials, which I had seen in Birmingham. The 1956 meeting was a big meeting - 200 or 300 - which went on for a few days. I was chair of one of the opening sessions. I was being recruited but said I wasn't coming so I was in an ambivalent position. There were people there saying, what the hell is this fellow doing here. But it was a very important meeting because at that time the first tools for evaluation had begun to appear. The scales had begun to appear - Jarvik had produced a scale for evaluating the effects of LSD - and Mort Kramer, the statistician was there. What emerged was the theme of experiment in context - the clinical experiment in the context of clinical observation and the refinement of clinical observation.

One of the odd things about the meeting is that none of the key organisers - Kety, Brady, Gerard, Lasagna - were psychiatrists, which seems extraordinary
Yes it was but we didn't have the kind of psychiatrists we have in place now - the Klein's, the Baldessarini's, who have made their names in trials - we didn't have them.

Actually by this time also the WHO had asked me to organise the study group on ataractic and hallucinogenic agents, which is not very well known but it was the first study group of its kind in this area. It was an international body and I wrote the preliminary documents and the final report for this in which you will find the same kind of philosophy. This was sent out to people, including to the Director of the WHO - Mental Health Section, Wolff who was an international specialist in addiction who wrote me back a letter which said literally that it sent my heart beating faster which was not

very good for me. The meeting took place six months later in Geneva. I wanted to thank him personally but was told he was quite ill. So I went to his flat and he was there with oxygen on, drifting in and out of coma. I have imagined since that he was referring to my vision which although confused broke through here and there and was a vision of the comprehensiveness of the field. Because even then I talked about the importance of subjective experience.

Let me pick up on all of this by asking where did the Macy Foundation meetings come from?
I don't really know. I have an idea that there was a spirit in the foundation who became intrigued in psychopharmacology. Macy funds were used to bring people together in whatever field and this was the modern field. I didn't attend the first one but I attended the second one, where I talked about the subjective LSD experience.

You had some LSD very early on?
Yes, we had one of the first samples from Sandoz and we decided to carry out an experiment in 10 subjects, just before the Xmas after I had come back from America. We decided to have a small dose - half a mcg per kilo which gave me a dose of 35 mcg. I was the first subject, Charmian was the second, Bradley was the third and so on. We did it using a throat microphone for subjective experience, EEG and stroboscobic photic stimulation done to 14 cycles per second. That is the only time I have ever had LSD. It was reported to the Physiological Society as an abstract. It was an astonishing introduction to this whole world which made it Holy Ground for me but also within two years made me and Charmian and Mayer-Gross write a letter to the BMJ advising against using this outpatient settings. I remember warning our authorities and the NIH about this. I remember an agent from the Bureau of Narcotics coming in and putting three sugar cubes on the table which he said each contained a 100 mcg of LSD which he had bought on the street in San Francisco and I said "My friends we have just seen the virus of the 20th century". I was partly responsible for the later restrictive rulings on LSD. Danny Friedman and I were on the committee that restricted its use.

Why?
Why? Because it was such extraorinarily powerfull stuff. We saw the way it was likely to be misused and then of course Haight-Ashbury broke out. I was very strongly opposed to its use. It was restricted at first to clinical trials. Grof and Kurland did some studies on dying patients where it did help like morphia or any other drug but this was in a restricted medical setting. I was never tempted to take a second dose because I had a feeling that this was something sacred and I felt that the sacred states have to be prepared for, practised, re-entry had to be monitored carefully. It was Holy Ground. I said right at the beginning, to Stan Grof as well, get away from the chemical prosthesis, there are inner mechanisms - there is an extraordinarily powerfull inner pharmacy which can be activated by physiological processes, particularly by breathing exercises. Since my medical student days, I have been interested in yoga practices, in Steiner exercises, in meditation and in breathing and of course art as mechanisms for activating these states. These are ways of healing and of repair and I think we should learn to use them independently of the prostheses of drugs.

This has been with me since my youth and I backed into psychopharmacology and contributed to it and to the theory of it but I essentially believe in the inner pharmacy,

inner healing powers which are innate, genetically encoded and activated by stress and injury. We may use a prosthesis temporarily but I am unhappy when I hear what Kramer and other people write about Prozac. The jury is still out on this. Some good and sensible people speak about it as a very important element in their lives. You should read Kay Redfield Jamieson's wonderfull book on all this.

The Birmingham area, with people like Sandison, became a hot-bed of LSD use for therapeutic purposes. Any ideas why?
I included Sandison in my WHO study group. Its use stemmed from his being courageous. He was the deputy superintendent of Powick Hospital and he came to me when we were working on the cats and he said he wanted to give a paper to the local society and I agreed. It was a rainy afternoon, only 7 or 8 of us turned up and he gave us this extraordinary account of this LSD work with schizophrenics and I felt I had listened to something very important and profound. Why ? - because the phenomena were so striking. He got some good results but it was totally uncontrolled experiment, so I was not convinced by the therapeutic outcomes but I was amazed by the productions and drawings and also by my suspicion that an amine, possibly serotonin, was in some way related to schizophrenia. I felt that I had listened to something very important. Then I included him in this very select WHO group that I convened. Everybody was very surprised at that.

There was a fork in the road around the late 1950s or early 1960s. LSD or that kind of compound were much more experimental psychiatric compounds, whereas chlorpromazine was for therapeutics and we've gone the therapeutic road it seems to me to the neglect of an experimental approach. Would you agree?
I would and just as we learned so much from morphia about the nature of pain, we can learn a great deal from LSD and this is going to come back. It is slowly coming back but I saw at that time the tremendous psychological damage that this drug, working in such minute doses, could produce. The idea that kids should be able to "drop acid" gave me the shivers. But as an experimental drug it satisfied the criteria I had from the beginning, David, it was a very precise tool just like the anti-cholinesterases. Stan Grof calls it the electron microscope to the unconscious. I totally support its use as a way of elucidating mechanisms of perception, of cognitive functioning, of recent memory and learning.

I was invited one year by Richards who got a Nobel that year to give the Harvey lecture, which was a black tie lecture. He asked me to talk about the work we were doing in St Elizabeth's. I started writing the usual thing and then turned to the question of the validation of subjective phenomena, so I changed the theme of the lecture and called it subjective and objective observation in psychiatry. I gave it to a very distinguished audience. A good many of the crowned heads of psychology and psychiatry in the New York area were there. I got glazed looks. Even Heinrich Waelsch looked a bit disheartened - you know what I mean - but in may audience was Fritz Lippman, Nobel in Chemistry, Paul Weiss one of the great neuroscientists. Three days later I got a letter from Paul Weiss saying this was one of the most extraordinary distinguished lectures he had heard, Fritz Lippman ditto and others. So I got an understanding from the physicists and chemists but not from psychologists.

My closing argument was for the need for a new symbolic system to describe subjective phenomena and for the training of special observers, whom I called intronauts to explore inner space with the same precision that we explore outer space. This would require long term investment in a group of trained observers and in inner space laboratories. The message was that if we establish such a group of observers and take this as seriously as anything else, then we can do something. At Feta now we have study groups on states of consciousness and we want to do what Schmidt did for neuroscience - to assemble the best people from all over the world. If you take this seriously you must take it off the street and put it into the hands of people who will treat it with the care and reverence that the Mexicans gave to mescaline. This is what experimental psychiatry should be all about.

This seems to be just what we are lacking at the moment - psychiatry has seemed to reduce to therapeutics only, which while it is of crucial importance it can't sustain the whole enterprise
Oh heavens no. It is the Queen of medicine to my mind. There isn't another subject with such immense potential. This is what it meant to Adolf Meyer as well.

On that point, has DSM-III been a major mistake because it strips away the social dimension to psychiatry and sees illnesses as categorical entities.
I agree with you but we had to do it because psychiatry had to take a Sears and Roebuck approach - biochemistry, yes we carry that item, animal behavior yes we carry that item. In the same way with phenomenology, yes we carry that now but this horizontal dimension has to go through education. If I had been at Hopkins long enough I would have organised training quite differently. People would have had to have a full range of training from anthropology to clinical psychiatry and psychoanalysis which was a mushrooming and lucrative industry here would have had to take its place. But when I came to Hopkins, the four analysts on the staff took me out to lunch and they said they'd like to tell me what they were doing. I listened to them very carefully and said I promise you that what you want will be respected and taught. So psychoanalysis had its place with neurochemistry and the other disciplines. Indeed I had a training analysis - 350 hours. It was a lot of time but well invested. I recognise the value of the discipline. The theory is lousy, its wrong but the process is okay.

What about the foundation of ACNP
A gleam in the eye of Ted Rothman who called Jonathan Cole and me and then along with Fritz Freyhan, Paul Hoch and Joe Zubin and a few others got together a committee for a preliminary meeting and then there was a meeting at the W.... Hotel which was the first meeting at which they elected me the first president. When the first bulletin of the ACNP came out, I summarised the committees I had created which went all the way from a committee for experimental science to a committee for government and industry. I outlined the purpose of the College in the first bulletin and ended with the piece from my presidential address where I said what I felt about the field. That piece was reprinted in the programme on the 20th anniversary of the College. Fred Goodwin and I were checking in and he said Joel that's a wonderful contemporary statement and I said Fred that's 20 years old.

Why did they pick you?
Because somehow in my discussions I tried to broaden the horizon, raise the sights, point out the connections and I was also in charge of the probably the most powerfull

center in the world at the time. St Elizabeth's was already beginning to show its scope and its strength - no university had anything like it. We felt exiled a bit. But I was totally surprised, genuinely totally surprised when I was elected. I was overwhelmed. I felt in a sense a deep responsibility. I felt that this is going to hit society in a tremendous way. We had the responsibility to put together the bones of a new science - a tremendous social responsibility.

My view was build soundly, build broadly and build models. I can give you a story about doubt. Bob Felix from NIMH came in one day and assembled his core staff and said I've got good news, I've just come back from the Hill and we've got $520 million to create community mental health centers. Bob, I said, $520 million, how are you going to do it? He said "we've got to spend it". I said Bob we haven't got a model of a community mental health center, let's do one in Massachusetts, one in Appalachia, one in California, about 5 all together and let's see how they go. And he put his hand on my knee and said "Joel, you come from England, this is America, I tell you we've got the money, we've got to spend it" - more or less saying shut up and don't mess my thinking. And you know community mental health centers became a paradise for social workers. They didn't produce much research. Then it became the politics around money, which is something I've kept out of totally - I've kept out of the APA completely. But the ACNP flowered from then onwards.

Your next move was to Hopkins.
Yes. I was surprised when I was offered the Chair at Hopkins. There was a tremendous conflict over whether to leave or not. They approached me two times. I nearly left for other reasons. Jonas Salk was building the Salk Institute at that time at La Jolla in California. A magnificent institute built by Lou Kahn one of the great architects of our time. He and I were close friends. I remember talking to him in the early 60s and he said I've $40 million dollars, I'm building the Institute of my dreams, standing in La Jolla looking over the Pacific. I'm going to have the humanities on one side and science on the other. I want to build the institute that will foster a conversation between them and have an impact on the world - because he was a dreamer. Next thing I knew he was sending me photographs of the models, then he invited me out with Charmian. Jonas and Lou Kahn were selecting the slabs to build the institute in - they were lying there on the edge of the Pacific. Then I was sent around the world to interview with Bronowski and I was apparently passed to be a founding father of the Salk Institute. Charmian and I went out to pick a house in La Jolla which was dead cheap in those days. This was paradise. I came back to find a third letter from Hopkins, this time from Eisenhower, Ike's brother, who was president at Hopkins - Dear Dr Elkes, I believe we have now met all your terms for acceptance... I went through agony with Charmian for one horrible day. Salk is totally new, with an endowment for pure research, the other one is practical, will involve teaching, is down in an inner city in an old building. I don't know to this day I don't know whether I was playing safe or my sense of social responsibility won out - it was probably a bit of both. Hopkins was the best chair in the country and I could influence more people. Salk was at that time an uncertain quantity. I chose Hopkins and I called up Jonas and told him.

At Hopkins I found a rather old institution. Brilliant people around but it didn't have the energy, efficiency and verve of the NIH at the time. I started to clean out a bit of deadwood and bring in Joe Brady, found Jerome Frank in it, John Money, Horsley Gant, Kurt Richter who worked on biological clocks was there. The dream as before

was to build a new type of psychiatrists who would be a good clinician and a good scientist. The prototype of that at St Elizabeth's was Floyd Bloom and then at Hopkins it was Sol Snyder. He came to me from Julie Axelrod. I got him a residency and by the second year he showed his aptitude in biochemistry, so I went to Paul ??? who was professor of pharmacology and asked could we set up a lab for this extraordinarily talented man and we did. Then I had a fight with the Director of Training who just didn't see it - Dr Snyder has to see patients. I said no, it may take a little longer but he will do both. And Sol did the famous receptor work there, which by the way demonstrated the regional distribution of receptors and neurotransmitters confirming some of my early hypotheses. So many other generations of excellent clinical scientists have gone through. I would say between my labs in Washington and Baltimore, more than forty people world-wide have gone through and assumed leading positions - pharmacologists and psychiatrists. We began to set this pattern and now no-one is appointed to a chairmanship if they aren't both psychiatrists and psycho-pharmacologists or some other scientist. The pattern of being both a good clinician, first and foremost, but also a respectable scientist.

When I retired from Hopkins, I went to McMaster because I was interested in medical education. I helped create the area of behavioral medicine there. Then I went to Louisville, Kentucky, for a lecture in which I suggested we should do something about health education in medical students and the president came to me afterwards and said "well why don't you do it in Louisville?". I said "well I came to give a lecture" and he said "well why don't you come to dinner?" and after that he said "well that's a recruiting dinner, we want you here". So I started a health awareness program in medical students which has gone great guns. It was essentially a program to give life skills to students before they entered the obstacle race of medical education, including nutrition, exercise, relaxation, listening skills, biofeedback and so on all in an experiential way. Mobilising the inner pharmacy. All done as a voluntary exercise but yet the whole class turns up a week early each year to go into the health awareness program.

My role at Feta now, as a visiting fellow at the Mind-Body Institute, which is a very large institute, endowed by Mr Feta who invented the directional antenna which made cable television possible. He was a deeply spiritual engineer who was convinced that there are bioenergetic fields in man and he established an institute to study the mind-body-spirit connnection and there we have run a major series on the healing of the mind which has been a best seller, seen by 5 million people. We're doing one on the arts and one on the teaching of teachers in these life-skills. So I have been going full circle from the dreams of my youth to the dreams of my youth back to the inner pharmacy by way of all the impedimenta of the outer pharmacy.