IN THE BEGINNING IN PARIS
THÉRÈSE LEMPÉRIÈRE

When did you join the department of Psychiatry in Paris?
I began in Sainte Anne in the service of Professor Delay in 1950 as an intern - a resident. It was my first job in psychiatry. I stayed there for a year and after that I went to the Salpétrière to finish my training in neurology with Alajouanine and Garcin and in child neuropsychiatry with Michaux. During this year in Sainte Anne I had the chance to get to know psychiatry before the arrival of the neuroleptics. At that time we were giving a lot of electroshock and the Insulin Coma treatment of Sakel but if all of that failed one felt very helpless.

Were you with the university department or were you in the hospital?
I was in the service of Professor Delay which was the only university service of psychiatry in the hospital. I was working with Deniker who at that time was a young assistant.

How many patients were there in the hospital at the time?
In the service of Professor Delay there was approximately 200 patients. Altogether in Sainte Anne there were approximately 1000 patients. The services were overcrowded and living conditions were very mediocre. The medical heads of departments were competent practitioners but they were working in very difficult conditions with few collaborators. Sainte Anne was the only psychiatric hospital within the boundaries of Paris.

How many patients did you have to look after?
Approximately 50 but this was under the supervision of Deniker. In Delay's service, which was a university service, the number of medical people was much greater than in other services.

There was also Dr Harl. His name is on the first papers about chlorpromazine.
Jean Marie Harl was one of my friends. We had met first in the faculty of medicine. He succeeded me as a resident in the service of Delay and it was he who made the first clinical studies of chlorpromazine with Deniker. He was a good clinician and he had an excellent rapport with patients. When his residence came to an end he did not continue with a hospital career. He turned instead to private practice in psychiatry where he was very successful. However he died young in a climbing accident in the Alps.

When did you become aware of chlorpromazine because you weren't actually there when they began to give it?
I remained in contact with the service of Professor Delay and I was aware of the studies with chlorpromazine. We were very quickly able to use the product and I can recall that we had already used it during the summer of 1952 when I was the resident in the Salpétrière in child psychiatry. That service had access to a number of beds for adult patients and the Chief of service, Michaux, was very interested in this new medicine. Very quickly therefore we were able to establish for ourselves the activity of the product for patients with schizophrenia or mania. I can recall that we used to dread phlebitis. There were a number of cases partly perhaps because it was the practice to let patients remain in bed because of hypotension.

When I returned to Sainte Anne in 1953 to Professor Delay's service, Largactil was clearly already in widespread use. Very shortly afterwards Reserpine came and we were able to make a comparison between the two medicines. I remained there in that service initially as an assistant and then later as Associate Professor until 1970. Then I left to become head of the university service in a new hospital in the suburbs of Paris the Hospital Louis Mourier at Colombes. During all this period I participated personally in trials with a number of psychotropic drugs.

Pierre Deniker when he talks about the discovery said that for a while during 1952 at least, people were not very interested.
In the milieu in which I was, at the Salpétrière, interest was immediate but this was a university setting. It is true that in general psychiatric settings the first publications on chlorpromazine did not generate a great interest. There was scepticism and a certain reluctance to admit that chlorpromazine was not a simple sedative like chloral or the barbiturates. You must remember that at this time we used to do a great number of sleep cures for the most agitated patients. Delay and Deniker had difficulty in persuading people that chlorpromazine had some antipsychotic specificity. As so often when a new innovation comes along, it was the younger psychiatrists who most quickly appreciated the importance of the new treatment. In many cases it was the residents who introduced chlorpromazine into the services where they worked.

The introduction of the neuroleptics transformed the atmosphere in clinical practice, it greatly reduced the states of agitation, it reduced the number of days that people remained in hospital, these are all things however on which I don't need to insist. Psychiatrists generally received it as a major step forward in practice but it didn't lead to a complete change in their way of thinking. They already had the idea that disorders such as schizophrenia or mania had a neurobiological substrate - at that time one didn't talk about brain biochemistry and the fact, therefore, that an antipsychotic treatment had been discovered didn't come as a huge shock in contrast to the situation when the effectiveness of the first antidepressants was established - then many psychiatrists were greatly troubled because this did challenge their ideas about what depression was.

I can see what you are saying but even in the case of people who are depressed, there was the example of electroshock treatment which was working and Jean Delay had tried dinitriles and also isoniazid so obviously he thought something could happen.
Jean Delay had already the idea that mood disorders whether mania or melancholia were influenced by a biological disorder. In his book which appeared in 1946 he had already laid out his views on the possible disorders of mood. He had worked a great deal on the biology of electroshock and he was interested, without having any preconceived views, in all agents which were capable of modifying mood.

The majority of French psychiatrists however were not particularly interested in biological psychiatry. The dominant trains of thought at the time were psychoanalysis and social psychiatry. Even though they were prepared to admit that electroshock was efficacious in melancholia, many psychiatrists thought that the majority of depressions were neurotic or reactive and were caused either by

unconscious conflicts or unfavourable living conditions. They had great difficulty admitting that imipramine could work as well for these kinds of depressions.

Also you must remember that psychiatrists at this time who thought that there might be a biological disorder in depression thought that this would be an endocrine disorder. They suspected that at some point someone would discover an effective hormonal treatment.

Was Jean Delay closely involved with the work? For instance if we look at the first symposium on haloperidol at which your work was presented, the presidence d'honneur was Divry but he was not involved with any of this work at all. Even though his name was on a number of early articles. Was Delay more than a presidence d'honneur in the department?
Jean Delay had great intellectual breath and he was a very creative spirit. In addition his medical training, and you have to remember he was a professor of medicine before he became a professor of psychiatry, and also his psychological training, where he was a doctor of philosophy, gave him openings to many different domains of thought. He immediately understood the interest in chlorpromazine and followed this up quickly with other studies undertaken in his service. He was not the hands-on person in the sense that he did not spend time everyday at the bedside of the patient but he did make a point of seeing the difficult cases. He was also tremendously stimulating for his co-workers and he clearly indicated to them the direction in which research should go.

In addition to his interests in psychopathology, Jean Delay was also concerned about what the advances in psychopharmacology might teach us about the workings of the mind and also about mental illness. As he had done with electroshock, for instance, he used the antidepressants to analyse depressive syndromes. His classification of psychotropic drugs reflects well his psychopathological orientation which was one that had been inspired by Janet.

How do you weigh the respective contributions of Jean Delay and Pierre Deniker?
Deniker was very involved in both clinical research and in the care of patients. He personally saw many patients and supervised very closely the work of the residents. If we take the case of chlorpromazine he was the one who supervised the clinical trials from day to day. Delay looking at the developments from a greater distance immediately understood the importance of the results. He became very quickly convinced as did Deniker that this was a product with original properties and that we should pay great attention to it.

Did you know Laborit?
Not very well it was Deniker and Delay who principally knew him. I met him a few times at meetings for example at the international congress on chlorpromazine which was held in 1955. This was the first time that I met him.

What did you make about all the fuss about the discovery of chlorpromazine?
I think that Laborit had a very good feeling for the potential interest for psychiatry that chlorpromazine offered. He himself however was not a psychiatrist and had never tried the product out in a psychiatric patient. I think that the clinical studies that

Delay and Deniker did really were the turning point because they immediately noted the antipsychotic activity and all that it was about this drug that made it original and distinctive compared with other sedatives and tranquillizing agents.

You also must not forget the researchers in Rhône-Poulenc Spécia who already had produced antihistamines before chlorpromazine. In the 10 years before the arrival of chlorpromazine there already had been clinical trials in psychiatry with a number of antihistamines. So this idea was in the air.

The 1955 congress. What can you tell me about the atmosphere of that meeting?
This was the first great international congress to be organised on the subject of psychiatric treatments and it came about because of the development of chemotherapy with chlorpromazine. At the meeting there was also talk about Reserpine and sleep therapies. At the meeting the audience were mainly psychiatrists because at the time there were no psychopharmacologists. I can remember very well the atmosphere. I can remember my impressions at seeing people like W. Mayer-Gross, Manfred Bleuler or H R Rümke. At that meeting I met for the first time Fritz Freyhan and Heinz Lehmann. The psychiatrists who had been invited to the meeting all had good experience with neuroleptics. Many of them had already treated hundreds of cases. The discussions therefore were very interesting and there was a certain consensus about the effects and side-effects of the neuroleptics. Mayer-Gross was already insisting at this time on the need to move beyond empirical studies to controlled studies.

When you came back from the Salpétrière to Sainte Anne you got involved in a trial to compare chlorpromazine with reserpine. This came out in 1954 within weeks of Nathan Kline's Study but your study is rarely mentioned in terms of the discovery of the psychotropic effects of reserpine. How did it compare to chlorpromazine?
Our publication dated effectively from July of 1954. It was the second in the world. We followed up the studies with reserpine during the succeeding years. The similarity of the antipsychotic effects and side-effects of both it an chlorpromazine led Delay and Deniker to their definitions of neuroleptics as a novel class of therapeutic agent. We considered at the time that the activity of reserpine was possibly superior to that of chlorpromazine for chronic schizophrenics.

Why did it fall out of use?
Well there were difficult side-effects. It caused drooling, akathisia and cardio-vascular difficulties. It was also dangerous to use with electroshock. Furthermore there was a risk of depression. The prescription of reserpine began to fall progressively following the appearance of other neuroleptics and in particular haloperidol.

Did you see people with schizophrenia become depressed when they took reserpine?
No I don't remember seeing people with schizophrenia who were on reserpine become profoundly depressed - that is to say melancholic. A certain number of them were dysphoric. But I had the occasion to treat a number of patients who had become depressed with reserpine for their hypertension.

When some of the early neuroleptics were used, in particular prochlorperazine, people began to describe some surprising what we now know are extrapyramidal syndromes.
It was the psychiatrists in Lyon, Broussolle and Dubor, who first drew our attention in August of 1956 to certain atypical psychomotor phenomena in patients taking prochlorperazine, a certain type of spasm, trismus and athetosis.

They described these things as somewhat hysterical manifestations which seems surprising now.
Not quite. They talked about the hysterical effect of the medicines. In effect they were suggesting that the patients appeared particularly suggestible. They noted that they were able to suspend their crisis, at least partly, if it was asked of them. In the case of others if a patient in a room had a crisis this appeared to be able to trigger off a crisis in another patient who was also taking prochlorperazine.

Was it akathisia they were describing?
No, these were dyskinetic crises. Akathisia had already been observed with chlorpromazine and in particular with reserpine. We had already in addition remarked on the oculogyric crises.

When were these syndromes first discussed?
It was quickly appreciated that these dyskinetic crises bore similarities to the excitomotor phenomena that were observed in post-encephalitic Parkinsonism. In those conditions also patients appeared to present a particular suggestibility. Furthermore the use of the prochlorperazine raised some practical problems. It had been developed as an antiemetic agent because its neuroleptic properties appeared at least in the laboratories to be somewhat weaker - although this was not later borne out entirely. It had been prescribed for both children and pregnant women. The appearance of dyskinetic crises raised diagnostic questions because they did not immediately associate what was happening with the taking of the medication. With children the immediate thought was that they had an encephalitis for instance. I can also tell you the story of what happened to a secretary of one of my former heads of department who was a neurologist and not a psychiatrist. The young woman who was pregnant was taking prochlorperazine for morning sickness. She presented with paroxysmal contractions and trismus. She was hospitalised immediately in the belief that she had tetanus. The problems however cleared up 24 hours after the medication was halted.

How troubled were you by these dyskinetic reactions? Did you think you could be doing a serious injury to the patients?
For patients in psychiatric hospitals this was not a serious problem, the psychiatrists and hospital attendants were well acquainted with dyskinetic crises and were able to reassure the patient. You could give an anti-Parkinsonian injection which would bring the problem to an end very quickly. The principle diagnostic problems occurred at home when a general doctor prescribed a neuroleptic as a tranquilliser or as an antiemetic agent without being fully aware of the possible side-effects.

Was it only later with drugs like Haloperidol that these effects became more common?

With Haloperidol and Thioproperazine these effects were frequent but not more frequent than with Prochlorperazine.

One of the reasons to come to interview you was because Paul Janssen has said when he got Jean Delay to use Haloperidol that the person he used to contact to find out what was really going on was you. He did not ask Jean Delay or Pierre Pichot as he felt you were the person who really knew what was happening with the drugs.
At this time I was an assistant and was already well acquainted with the first neuroleptics and those that came after such as levomepromazine, thioproperazine, acepromazine etc. This was in 1959. The experiments with Haloperidol were interesting because it was a new family of neuroleptic drugs and we were interested to compare it with the phenothiazines and reserpine. I became very quickly aware that it was a neuroleptic that was extremely potent. Initially there were problems because one had to feel ones way to getting the right dose. There were parkinsonian syndromes that appeared more quickly and were more severe than with chlorpromazine and we began to use more anti-parkinsonian drugs. But once we had got through the difficulties at the start in trying to find the dose, the product appeared to us to be very easy to handle.

When you were doing the trial with the haloperidol, did you think that it was an improvement on chlorpromazine?
Yes indeed, it had a quicker onset of action and was more potent in acute psychoses. Clearly there was the question of the dosage but one had the impression that this was a neuroleptic which would in due course in some areas at least supplant chlorpromazine.

You described how the secretary of the neurologist you knew took prochlorperazine and had an extrapyramidal crisis, that kind of vignette brings home the reality of what was happening. That people were not expecting these things. Is there anything you can remember with haloperidol that brings home what was different about it? Are there any patients that you can see in your mind's eye which illustrate what haloperidol meant?
One of the things which took us by surprise was its rapidity of action particularly on hallucinations. For example I remember one female patient who had been chronically delirious and very hallucinated whose voices disappeared in a few days. She said to us that they had cut the telephone wires. She herself was very surprised at what had happened.

When you had patients who responded like this did you go back to Pierre Pichot and Jean Delay and sit in their office and ask them to explain to you what was happening?
Yes indeed. We discussed all this frequently. In fact there had been a very famous psychiatrist during the period 1920 to 1930, De Clérambault. He had a view, a very mechanical view, about chronic hallucinatory delusional states and had proposed that their basis lay in certain small cerebral micro lesions - these provided a focus of irritation which gave rise to mental automatisms and hallucinations which were the building blocks of the delusional state. Along with Delay and Pichot we discussed the ideas of De Clérambault precisely because of this hallucinolytic effect of Haloperidol and the implications of this for delusional states.

What answers did you come up with - that De Clérambault was right?
I think that given all that has been now uncovered about the biology, biochemistry and neuroanatomy of schizophrenia that De Clérambault was on the right road. His ideas perhaps appear very simple to us now but in sixty years time I am quite sure that our ideas will appear equally simple.

Who did you discuss these issues with the most?
On the implications for psychopathology I discussed most with Delay and Pichot. We also had in Sainte Anne Thuillier and Nakajima and with them I discussed the questions of biochemistry and psychopharmacology. I also had a chance in the course of daily clinical work to discuss clinical problems with Deniker and with a number of other young psychiatrists such as Ropert and Ginestet.

Was there any feeling that Haloperidol was Pichot's drug and he wanted it to do better than chlorpromazine because of a rivalry between himself and Deniker?
No. Pichot was objective and in our publications we only reported that which had been established. Thirty years on you can see that haloperidol is in widespread use. It has become the reference neuroleptic for many control trials. We did a great deal to explore the psychotropic properties of haloperidol, using in particular the rating scales of Wittenborn which enabled us to show that it did not have a particular action against the negative mood states that go with schizophrenia. Pichot was always very interested in both quantitative psychopathology and in psychometrics.

Did you meet Paul Janssen around the period 1959-60? What was he like at that time?
I can remember having already met him at several meetings. I got to know him better when we did our studies with haloperidol and then later with trifluperidol. He is a man with whom it was easy to get on, who was very down to earth and direct. He already had a reputation of a first class researcher. It was his laboratory which had also discovered Palfium. When he suggested to us a clinical trial with Haloperidol we thought that since it was he who was proposing it and that he had already made a screening of the drug in his laboratory that there was a good chance that this was an active drug.

There is a very French idea, and I don't know who is responsible for it that the neuroleptics were not all the same that there were sedative neuroleptics and disinhibiting neuroleptics. Do you know who had this idea first?
I think that the first people to talk about a disinhibiting effect were Broussole and Dubor in their first communication on prochlorperazine in 1956. The first classification of neuroleptics was put forward by Lambert in 1960 and Revol. This was a linear classification in the sense that on the left were sedative agents and on the right incisive agents that is to say antipsychotics.

As far as I can remember French psychiatrists have always had the idea that neuroleptics are not interchangeable. This was already the idea of Delay and Deniker who put forward a series of increasingly complex classifications. The first one was in 1961. These typologies generally tried to establish a relationship between therapeutic effects and secondary neurovegetative or extrapyramidal effects.

The concept of a chlorpromazine equivalent which was put forward by Davis and Ban always seemed to us to reductionist and was never accepted in France. In the USA, psychiatrists had access to much fewer neuroleptics than we had in France. This may have played a part in leading to a divergence of opinion. The arrival of the benzamides, for example sulpiride reinforced for us the idea that it was possible to have "different" neuroleptics. I think the Americans are now in the process of revising their position because of the atypical neuroleptics such as Clozapine.

Do you think that sulpiride is different? Where did it begin to be used? Were you involved with any studies on it?
Sulpiride was marketed in France in 1969. I don't know who did the first clinical studies. It was a product which had a curious career. It had been widely used by general physicians for nervous problems of a functional nature. In psychiatry it did not take long to begin to mark out its distinctive properties. The patients themselves appreciated it a great deal because it was much less sedative than other neuroleptics and did not give them the same locked in feeling. In an empirical fashion it became clear that it had a particularly interesting effect in schizophrenias with deficit states and this was confirmed during the 80s by some well focused studies. The fact that it was a disinhibiting antipsychotic with minimal extrapyramidal effects made it an atypical neuroleptic.

Outside of France everybody has heard of Jean Delay, Pierre Deniker and Pierre Pichot but not Pierre Lambert. Why?
Pierre Lambert was head of department in the psychiatric hospital Bassens in Haute Savoie. He was not a professor and because of this he had much less influence with international audiences. His publications almost entirely appeared in French reviews and I think that this explains why his work is not known very widely outside of France. He was however an extremely good clinical observer with enormous experience in the use of psychotropic agents. He was also a psychoanalyst and he brought a psychodynamic dimension into his thinking about the action of these drugs.

One of the other Rhône-Poulenc compounds that Lambert worked on earlier was trimipramine (Surmontil).
Yes indeed. In France we have always had an interest in therapeutic cocktails whereas in England you are much more likely to use monotherapy. When we had imipramine for instance as an antidepressant it was common to use it in conjunction with a sedative neuroleptic such as levomepromazine, with results that appeared very satisfactory to us. From this came the idea of some of the researchers in the laboratories of Rhône-Poulenc Spécia that it would be a good idea to produce a drug, trimipramine, which would have in its molecule the nucleus of imipramine and the side chain of levomepromazine. The psychiatrists in the region of Lyon and in particular Lambert were the ones who made the first studies with this.

Lambert was also involved with sodium valproate?
In France, we have had two very similar products for a long time, the valproate of sodium (Depakine) and valpromide or dipropylacetamide (Depamide). Both of these were anti-epileptic but valpromide was also used as a thymoregulator. In addition valpromide was a pro-drug, of which 80% was transformed into valproic acid and the

properties both pharmacokinetic and psychotropic of these two products were somewhat different.

Lambert did studies with valpromide as an anti-epileptic and observed that in addition to anticonvulsant effects this drug had a beneficial action on some of the character difficulties and mood problems of his epileptic patients. This gave him the idea to study valpromide in mood disorders without epileptic complications. His first publication dates from 1966 but there was an even more important one in 1968. Since then valpromide has been very widely used in France in association with neuroleptics or Lithium during episodes of mania but also as a prophylactic treatment in bipolar mood disorders.

In the late 1950s and the early 1960s there was a real idea that drugs which were useful for epilepsy might be useful for psychological disorders too. The whole idea of the interface between epilepsy and psychoses was being explored. Does that seem right?
The idea of a relationship between epilepsy and psychosis is a very old one in both German and French psychopathology. It was drawn from clinical experience and had given rise to a great number of theoretical formulations. The shock therapies with cardiazol or electricity depended initially on the idea of an antagonism between chronic psychoses and epilepsy. In addition a number of people had proposed that there were resemblances between epileptic paroxysms and the paroxysms of acute psychoses and of mood disorders. I think Lambert initially began from clinical observations and knew of the beneficial action on mood of Depamide on epilepsy and went on from there to study this effect in manic depressive patients. I don't know if the Japanese psychiatrists, Takesali and Okuma who were the first to investigate the action of carbamazepine in mood disorders around 1970-72 had a theoretical presupposition. After all that then there was the work of Post and the North Americans who became interested in clonazepam and also in valproate.

Can I ask you about Anafranil? What did you think of it and when did you begin to use it first?
I did my first studies with Anafranil with Pichot and our first publication was made at the 4th World Congress of Psychiatry in Madrid in 1966. We had at this stage already treated 50 depressed patients and we had formed a very favourable impression of the product. We have used it a great deal since and our first positive impressions have been confirmed. I can remember advising Geigy to market it in France. I certainly had the impression that it was a good drug.

At the same Congress, Sigwald and Raymondeaud had made a communication on intravenous perfusions with clomipramine in eighty depressed people with good results. In France, the practice of intravenous perfusions with antidepressants was already current, at that time. Delay and Deniker had already written an article about this matter in Encéphale.

What was it about the product that made you think it was a good one and can you remember anything about why you thought it was so good?
Well our first work consisted of open studies. I think that the experience of clinicians is extremely important. We had already done studies with medications that had been presented as potential antidepressants but these were either ineffective or

were very badly tolerated and were not developed. Furthermore we had had the experience in practice of using imipramine, the MAOIs, and amitriptyline. You could therefore make comparisons. The opinion of the patients was also very important. When you have a good product, patients are more likely to adhere to their prescriptions. When they leave hospital they came back for research to follow-up whether they remained well or whether there had been a relapse. Anafranil was not marketed in France until 1967. I was quite sure however that it was a good drug.

Did you get the impression that Geigy weren't very interested in this drug?
They already had developed Tofranil. They had both Pertofran and Anafranil in clinical trials. They were not certain that they were going to develop all three. Finally Pertofran was marketed in 1966 and after that Anafranil in 1967.

You described anti-obsessional effects of Anafranil but Guyotat from Lyon also did so. Did he talk about these effects first or were you talking about them first?
This is Jean Guyotat and his collaborators. Guyotat was professor of psychiatry at Lyon. In their publication which appeared at the 64th congress of Psychiatry and Neurology in the French language, which was held in Dijon, in July 1967, they insisted that Anafranil had an action in obsessional neurosis. They reported on 12 cases that had been treated with 10 either good or very good results. They also noted that this effect did not wear off even though certain patients by then had been treated for over a year. They concluded that "in obsessional neurosis, it is the medication that is most reliably active that we have yet seen on the most troublesome symptoms of this disorder"

The use of Anafranil in obsessional neurosis spread rapidly in France. In a congress organised by Geigy in 1970 on "Anafranil in conditions other than depression", which was held in Palma in Majorca, there were a number of communications in French on its use with obsessional patients from Michaux, Gallot, Scherrer and myself. In this period it seemed accepted that Anafranil was more effective than other antidepressants such as imipramine or iproniazid and that its effectiveness did not depend solely on its action on an associated depressive state, that the patients relapse frequently when treatment was halted but that the effects of treatment did not wear off in the long term. I myself had followed up patients for over five years then. When I retired in 1993 I was still looking after patients who have been on clomipramine during this whole period. It had enabled them to live in a reasonable way during almost 30 years. Before this they would have been seriously incapacitated. The appearance of evidence that clomipramine had an anti-obsessional activity was very intriguing for the psychoanalysts and a great number of psychodynamic explanations were put forward to account for this. I must also say that during the same years a number of French colleagues were in the habit of treating obsessional neuroses with large doses of Periciazine (Neuleptil), a sedative neuroleptic which had been widely used to reduce the aggressive and personality disordered manifestations. On the basis of this there were theories that this medicine might have a selective action on the "sado-anale structure". Neuleptil, however, did not have a very long career for this indication.

What can you tell me about Buisson and isoniazid?

Jean Francois Buisson was of my generation. We were residents together with Delay. Delay had the idea because of his awareness of the beneficial effects of isoniazid on the mood of patients with tuberculosis who had been treated with this medicine. He proposed to Buisson that he should do his thesis studying the effects of isoniazid on depressed patients. The results were interesting.

But the odd thing is why with the results they had with isoniazid did they not say - we have found an antidepressant?

Yes you would have thought that they might have made more of this.

Why not. In 1952 they had shown it was good for people who were depressed but Pierre Deniker and Jean Delay all say that Roland Kuhn and Nathan Kline discovered the antidepressants six years later.
I think that the results they had were somewhat inconsistent. They were not decisive. It may not have been much superior to other drugs which they were using at the time in asthenic depressions such as the amphetamines. I believe that isoniazid is not a monoamine-oxidase inhibitor and that in this sense it is different to iproniazid. Perhaps it is only a psycho-stimulant?

We have mentioned a few other people like Harl, Buisson. Can I ask you about Thuillier. My impression is that he was one of Jean Delay's most important protégés. Then he left. What kind of person was he?
He was a dynamic extroverted individual with whom I got on very well. He had trained both as a pharmacist and as a psychiatrist. He ran a number of studies with animals and worked a great deal with the first neuroleptics. He had lots of ideas but did not have the means to study them all in detail. The laboratory was not very well equipped. I think that he left the service because he didn't have the possibility of a further career in INSERM or at the university. After that he entered a pharmaceutical company laboratory. But at the same time he also did a lot of other things. He occupied himself with a portrait gallery. He also wrote books which had some success among which was one about Charcot.

Who were the other important people in Sainte Anne, at the time?
With Delay there was a great number of other people who came from very different backgrounds. This was always fascinating. There was an active department of neuropathology under Brion which, during the 1960s, did important work on Pick's disease and Korsakoff's syndrome. These studies are classics. There was also a department of psychotherapy where a great number of reputable psychoanalysts worked. From 1953 through to 1963 Jacques Lacan used to come each week to give a seminar with the presentation of a patient from the service. Because of the reputation of Delay and Deniker following the discovery of chlorpromazine there was also a constant influx of foreign psychiatrists who came to train in psychopharmacology. Many of these became eventually eminent practitioners or academics in their own country.

There was also at that time in Sainte Anne many other psychiatrists who played an important role in the development of ideas and who influenced the younger generation. For instance, Georges Daumezon, who was a head of service in Sainte Anne, was a pioneer in the movement for the reform of psychiatric institutions. This

was a very vigorous development in France immediately after the War, which was brought to completion with the progressive establishment of sectorisation. There was also Julian de Ajuriaguerra who, up till his departure to Geneva in 1959, conducted his reseach at the Henri Rousselle, an institution which was included within Sainte Anne. He influenced younger psychiatrists by his innovative teaching in the fields of neuropsychology and developmental psychology. Above all there was Henri Ey, who had a huge influence both nationally and internationally. He was the secretary general for the First World Congress of Psychiatry. He also directed his own society - Evolution Psychiatrique - which brought together a number of psychiatrists and psychoanalysts and faced them with issues on which there was a divergence of opinion. Henri Ey was the Head of Department of the hospital at Bonneval, 120 kilometres from Paris. He used to come every Wednesday to Sainte Anne to conduct a seminar. These seminars were very popular with younger psychiatrists. At these he developed his ideas on psychopathology and in particular his theory of 'organo-dynamism', which greatly influenced French psychiatric thinking in the years between 1950 and 1970. The library at Sainte Anne, where he gave these seminars is now called the Henry Ey Library.

Was there any hostility to those of you who were working in psychopharmacology?

No, not during the first few years. The chemotherapy of mental patients became established progressively in the practice of psychiatry to some extent throughout all of France. There was no hostility at that point in time. Rather there was an interest although perhaps not a massive conversion to biological psychiatry. Psychoanalysis or social psychiatry remained the major attraction for most psychiatrists. The problems began with the anti-psychiatry movement which culminated in 1968 but it remained influential right through to 1975 and 1980. At that point in time there was rejection of all biological treatments and in particular both shock treatment and the neuroleptics and there were a great number of conflicts in clinical practice. I think this was even the case in Great Britain.

One of the things that must have begun to happen with the new medication was out-patient psychiatry?

In Sainte Anne and in particular with Delay there was already an important consultation service. With the arrival of chemotherapy, the levels of consultations went up enormously. It also became necessary to follow-up those who were discharged from hospital and in addition we had to accept a huge influx of new patients who were sent by general physicians who had become aware that it was now possible to help people who were depressed.

When did you begin to realise that you were going to have to educate people, to train them to use these new treatments. Did you have to do much lecturing on how to use the treatments?

It was particularly in the case of depression that it was necessary to make an effort to educate general physicians. Training in psychiatry in the course of medicine at the time was very brief. It was necessary therefore to teach clinicians how to recognise and treat a case of depression. There was a great deal of postgraduate medical education needed. It seems to me that in Great Britain the education of general physicians in this area was better than in France at the time. Perhaps your National Health system was better prepared for this?

When did people begin to be aware that maybe the patient did not have to come into hospital at all. That they could be seen in the clinic, given a prescription and sent home?
I think that these things developed gradually and the demand grew among patients and general physicians following the introduction of the antidepressants. You must not forget that in France private psychiatry developed greatly in the years 1970 through 1980. At the same time there was also put in place a sectorised public psychiatry service with dispensaries which were located in the towns and not in the hospital. As a result, in France the number of psychiatrists is much greater than in Great Britain. In actual fact there are 11,000 of us of whom more than half work in private practice.

What about the treatment of anxiety with drugs in France?
In France we consume a great number of both anxiolytics and sleeping tablets. In fact it is the country with the highest consumption of benzodiazepines in the world. Although there have been some restrictions on the prescriptions of benzodiazepines for the past few years following directives from the department of health, the consumption of these drugs remains at a very high level. We have frequently debated what the reasons for this might be. Generally it can be said that the French consume a great number of medications of any kind including alcohol. Another point is that medications are not expensive. Finally there is not in public opinion any great campaign against the benzodiazepines. As with a great number of other countries however there has been for more than 10 years now an important increase in the prescription of antidepressants but this seems to me to be very reasonable. I think this corresponds to a better assessment of patients who are depressed of whom a great number to date have not been diagnosed and accordingly not treated appropriately.