FORTY-FOUR YEARS of PSYCHIATRY & PSYCHOPHARMACOLOGY
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When did you begin your training in psychiatry?

I began postgraduate training on 2nd January 1953. But Paul Kielholz used to say I came into psychiatry already trained because as a schoolboy I was always interested in psychiatry. It had personal reasons. I had a brother 5 years my senior, who has a difficult personality. He did not cry for a week after birth. No one ever found any evidence of minimal or other brain damage but we think he was so much spoiled by the admission that he is under-privileged in spite of the fact that he was very intelligent. So I was confronted with psychiatry from youth. Also I lost my father from cancer when I was 7 years old.

1953 was just around the time when John Eugen Staehelin and Paul Kielholz had a meeting of all Swiss psychiatrists to introduce Chlorpromazine in Basel.

Yes, this Largactil-Symposion in November 28th 1953 [1]. From 1929-1959, Professor John Eugen Staehelin was the Chief of the Basel University Psychiatric Hospital and Outpatient Department. He had trained in Zurich under Eugen Bleuler. Staehelin was always at the forefront of introducing somatic therapies but he had an inhibition, like many descendants of ancient Basel families, against publishing something too soon. He with his co-worker Professor Benno Dukor were the first to introduce Insulin at the Basel University Psychiatric Hospital, but because of their common inhibition never published about it. So it has the name Cure of Sakel. Nevertheless he had approximately 100 published papers covering a large range of psychiatric problems. From his investigations in the field of encephalitis epidemica, he had observed that schizophrenics who passed through this disease and later developed a postencephalitic parkinsonism showed a decrease in psychotic symptoms. When chlorpromazine was introduced and the side effect of parkinsonism was observed, he along with Hans Steck, supposed that this neurologic syndrome might essentially be linked with an antipsychotic effect.

In 1952, Staehelin sent one of his assistants, Dr Felix Labhardt [2] to Paris to the Sainte-Anne Clinic, to look at the way they were using Chlorpromazine - RP4560. When he came back in 1953, Labhardt introduced Chlorpromazine on the orders of Staehelin. Kielholz was Oberarzt, that is Head Physician, the only one in the hospital at that time. He, Labhardt, Wilfried Rümmele, myself and others forced Staehelin to hold a Largactil-Symposion at the Friedmatt Hospital in Basel, the University Psychiatric Hospital, near the French border. The psychiatric hospital had been there since 1886. The University Outpatient Department was founded, after an initiative of politicians in 1921, in the town in 1923 and encorporated in the general hospital in 1977. I was later the Chief of that from 1.1.1968 until 31.8.1997.

What impact did Chlorpromazine have at the time?

It had an enormous impact. Staehelin favoured its use in schizophrenics over insulin, which it slowly replaced. In the first years of its application, most of the schizophrenics treated with it came out of their psychoses and gained more and more contact with social reality until they could be considered as cured. People who had been years in the hospital all of a sudden came out of their paranoid schizophrenia. One of the schizophrenic women, for example, who had the delusion she was a military colonel after four weeks of treatment with Chlorpromazine said: ”You do not have to call me colonel any longer. I know now that I was sick”. This effect continued as long as people took maintenance therapy with chlorpromazine. The paranoids and the

catatonics were the best responders - we could empty whole departments. But, and this was especially for the women, we had enormous problems to find them a new environment because their husbands mostly had divorced them. In Switzerland, it is allowed by article 141 of the Civil Code to divorce after 3 years of continuous illness.

Since the beginnings of his directorship Staehelin was an adherent of the open-door psychiatry and introduced in the early years of the use of chlorpromazine a system of day and night hospital. Patients on chlorpromazine maintenance therapy who were capable of working in town but still wanted to reside at the hospital were the "night" patients. Others who preferred to have an own apartment but only felt secure when they could spend the day at the hospital, were the "day" patients. They helped in the kitchen or the cleaning staff of the hospital and received pocket money. The night as well as the day patients did not live separately from the hospitalized patients, and by that they also exerted an activating effect on the latter. The whole hospital went through a transformation. The hospitalization time of the patients decreased enormously. Whereas, for example, in 1950 the average of days spent by the patients at the hospital was approximately 150 days, in 1960 it had decreased to 95 days. An optimism came into psychiatry which could never have been imagined before. Staehelin, in spite of being very prudent in his judgements always maintained a therapeutically very active attitude. When Paul de Kruif wrote his book “A Man Against Insanity” in 1957 about Dr Jack T. Ferguson, who himself had been a psychiatric patient but who was cured and later worked as psychiatrist using neuroleptics together with psychotherapy with great success, Prof. Staehelin, as a sign of his position in Swiss psychiatry and in research of neuroleptics, was asked to write the preface to the German edition

Soon after the introduction of the neuroleptics we, however, became aware of the fact that the schizoprenics often did not follow their maintenance therapy very long and therefore frequently had to enter the hospital again. The revolving-door phenomenon in hospital psychiatry had begun. Nevertheless, the patients spent less total time during a year at the hospital than before the introduction of these drugs.

We introduced - unofficially in 1953, officially in 1955 - group psychotherapy which allowed patients who were a long time in the hospital, to undergo a social training. There were ward groups and since 1957 specific groups with patients of the same diagnosis. In 1963, I began a special group with schizophrenics who were all treated also with neuroleptics, and published some work on this showing that these patients had a significantly smaller readmission rate and a shorter total hospital time after they were additionally taking part in group psychotherapy [3].

You’ve mentioned Felix Labhardt, can you tell me more about him and his work?
Felix Labhardt was the son of a professor of gynaecology and obstetrics at the University of Basel, Prof. Alfred Labhardt. He spent time in physiology before in 1951 he came to the University Psychiatric Hospital, under Staehelin. In 1952, Staehelin sent him for one year to the Salpêtriere and the Hopital Ste Anne in Paris, where Jean Delay was director, who along with Pierre Deniker, had already had great experience in using chlorpromazine. After having been in Paris for a year, Labhardt came back to Basel with a broad experience with chlorpromazine and was given by Staehelin the chance to begin using chlorpromazine preponderantly in

schizophrenics. He published his first results with this therapy at the Largactil Symposion 1953 in Basel. He proved statistically that chlorpromazine acted favourably in schizophrenics with a duration of psychosis of 1 to 5 years. Out of 46 patients, 22 (48%) showed an improvement and 19 (41%) a social or total remission. Only in 5 patients (11%) was there no positive outcome visible. In 106 schizophrenics with a duration of psychosis of more than 5 years he found a slight improvement in 28 patients (26%), in 42 patients (40%) a distinct improvement, and in 19 patients (18%) a total remission. Only 17 (16%) did not respond at all to this drug.

Labhardt was one of the main local organizers of the 2nd CINP Congress in Basel in 1960, although others received more of the recognition for the success of this meeting because they held official functions in the CINP organization. Nevertheless, many visitors came to Basel especially to learn from his large experience with chlorpromazine. One of them was Pierre A. Lambert, who wrote that “it was only after our contact with Prof. Labhardt from Basel, who confirmed the satisfactory tolerance of this dosage (500 mg per day) that the group decided to adopt higher doses. This change in the dosage of the therapy was, in all probability, the reason for the higher number of remissions observed subsequently.” In a later paper Labhardt published details of the results of the chlorpromazine treatment of schizophrenics between 1953 and 1955 at the Basel University Psychiatric Hospital. He examined the case reports of a total of 373 patients treated with chlorpromazine. He observed that a large number of patients, after having been treated successfully with this compound during the two observation years, suffered a relapse, which necessitated a new hospital treatment. More than half of the patients with a reoccurence of schizophrenic symptoms were due to noncontinuation of the maintenance therapy. Of the 107 schizophrenics with a duration of their psychosis of up to 1 year, 27 (25%) showed an improvement and 74 (69%) a social or total remission. Only in 6 (6%) patients could no amelioration be observed. In following 101 of these patients from February 1953 until February 1955, he could see that from them 46 (45%) had suffered a relapse - 18 (18%) in spite of the fact that they had apparently taken a maintenance therapy with this drug. Of the 185 schizophrenics which a duration of psychosis of more than 5 years, 46 (25%) showed a slight and 84 (45%) a distinct improvement. 30 (16%) were considered socially or totally remitted. Of the 160 patients with an improvement or a remission of their psychosis in the observation time of February 1953 until February 1955, in 93 (58%) the acquired state remained constant and in 57 (36%) a relapse occurred, 8 (5%) of whom had taken their maintenance therapy. He underlined that the results obtained with chlorpromazine, especially in patients with a psychosis duration of more than 5 years, were much better than in persons who were treated before with insulin, and that the patients who improved or were socially remitted developed mostly a totally new orientation towards social reality.

He was clearly a great pioneer of the treatment with chlorpromazine, but later also with other major tranquillizers such as levomepromazine, promazine, the butyrophenones etc. Because of his merits especially in the realm of psychopharmacology in 1957, he was nominated to be Head Physician and later on in 1960 Vice-Director of the Basel University Psychiatric Hospital. In the late sixties he was elected Professor of Psychiatry at the University of Basel, where he

remained until his retirement in 1988.

The picture of Labhardt would not be complete without a mention of his psychotherapeutic and psychosomatic interests and his mastership in the utilisation and theoretical considerations of the autogenic training of J.H. Schultz. At the hospital, however, the most prominent effect of his personality was his open, kind attitude toward the patients, but also toward the staff and all persons who had the pleasure and the privilege to be treated by him or to work together with him.

You mentioned Hans Steck also – he played an important role also.
Hans Steck came from an old Berne family. He got his psychiatric education partly in France and mainly at the famous Burghoelzli University Psychiatric Hospital under Eugen Bleuler in Zurich. From 1919 on he worked at the Psychiatric University Hospital of Cery, Lausanne, where he was appointed as one of the head physicians and later in 1925 the Assistant-Director.

Steck was always interested in neurology and especially in the postencephalitic mental and neurological disorders. From the beginning of his professional activity he paid close attention to the biological research of schizophrenia. Influenced by the neurologist von Monakow, who was one of his university teachers in Zurich, Hans Steck saw the main cause of this illness in a disorder of the circulation of the cerebro-spinal fluid and thought of it as a disturbance in the blood-liquor barrier in the concerned people. In 1931 he published a paper in which he developed his theories.

Because of his expertise in research, teaching and administration, in 1936 he was nominated as Director of the Lausanne University Psychiatric Hospital and Professor of Clinical Psychiatry there, later becoming the Chairman of Psychiatry. Steck stood not only in permanent communication with all Swiss psychiatric centers, but also with those of France. After World War II, he therefore had the privilege to organize the 1946 Congress of the Psychiatrists of France and the French-speaking countries.

When the major tranquillizers were introduced into the therapy of schizophrenics, from 1953 on he used chlorpromazine and soon afterwards reserpine. His special interest was now directed towards the extrapyramidal syndrome observed in schizophrenics treated with these compounds. He was reminded of the evolution he had observed in the cases of encephalitis lethargica and concluded that chlorpromazine as well as reserpine exert their action at the same place in the brain as this illness. This conclusion was for him also evident because he, like his friend and colleague of the time when both worked at the Burghoelzli in Zurich, Staehelin**,** had observed during his work at the Bleuler-Clinic in Zurich that chronic schizophrenics improved after later on having developed postencephalitic parkinsonism. He underlined that the parkinson syndrome caused by the major tranquillizers indicates that the localisation of their action is situated in the extrapyramidal and diencephalic system. He agreed with Haase of Germany, who had stated that the parkinson syndrome was the conditio sine qua non of the therapeutic effect of a prolonged cure with neuroleptics. Also he held the opinion that these drugs, by blocking the ascending activating reticular system described by Delay and colleagues cause the hallucinations of the schizophrenics not to

disappear but to lose their affective value. His view was that these compounds diminish the internal mental tension, leading to a reduction of aggressiveness and a protection against interoceptive and exteroceptive excitations.

Hans Steck, however, was not only a representative of biological psychiatry. He was equally interested in psychoanalysis and especially in the existential analysis of Ludwig Binswanger. He also accepted the conceptions of his head physician Christian Muller on the psychotherapy of schizophrenics, which were based on the work of Rosen. He supported his coworker in organizing in 1956 the first international symposium on the psychotherapy of schizophrenics at the University Psychiatric Hospital of Cery-Lausanne, where among others the well-known researcher in the field of psychotherapy of schizophrenics, Gaetano Benedetti from Basel, participated.

In addition, he was linked to the mental-health movement and engaged in the fight against alcoholism and prejudices against psychiatric patients. He promoted a social activation of hospitalized patients and sought the integration of as many patients as possible in occupational therapy. Also, he fought for an opening of psychiatric hospitals and was at the forefront in advocating the rights of psychiatric patients. Last but not least, he furthered schizophrenic art production. He discovered the artistic capacities of one of the hospital patients and published a paper on her (Aloïse) describing art therapy at his hospital.

Steck with his university and administrative positions, his research, approximately 90 publications, and especially his personal radiation and through his many disciples, has contributed enormously to the beginning of a new era in psychiatry, in which patients could hope to be helped effectively by both new psychopharmacological treatments and by psychotherapy, and to have the chance to be reintegrated in society. In spite of being mainly a representative of biological psychiatry and psychopharmacology, he saw the necessity of a combined bio-psycho-social approach to the psychiatric patient. It is, therefore, not by chance, that throughout his life he worked on a philosophical background with a broad understanding of his patients and a deep insight into the basic questions of human life.

I know you feel that Roland Kuhn's account of the discovery of Imipramine in the recent History of CINP neglected the contribution of Paul Schmidlin. Can we chase this?
Yes, Paul Schmidlin who worked in the firm Geigy gave Kuhn the drugs to be clinically tested. These drugs as I remember it were thought of as neuroleptics but Kuhn did not find a neuroleptic effect and reported to Dr Schmidlin that the trials are negative. However, Dr Schmidlin looked at this report and the protocols of the study, which were very thorough - Dr Kuhn is a very thorough man - and saw that it has an antidepressant effect.

What did he see that from?
From what I remember, he saw it in Dr Kuhn's protocol, where it was marked that some patients with schizoaffective psychosis in a depressive phase under treatment became manic. Dr Schmidlin insisted that Dr Kuhn must continue his examinations even though he did not want to. You can see something about this in a History of Psychiatry

written by a colleague of mine, Dr Thomas Haenel [4]. I will translate it but what he has written is not totally right because he did not dare to tell the whole truth: "A further remarkable progress in psychiatry was the discovery of an antidepressive medicament, Imipramine, Tofranil - and now comes what is not totally right - Roland Kuhn discovered in 1956 the antidepressive action of Tofranil, which was thought primarily as a medicament against schizophrenic psychosis. Also Paul Schmidlin, from whom the term thymoleptics comes, was essentially included in the introduction of Tofranil". Paul Schmidlin was a medical doctor who worked at that time at the firm Geigy - later Ciba-Geigy and now Novartis.

Tofranil was given to Kuhn in 1956 but also to us, to Kielholz and myself. We published our work on this in 1958 in the Swiss Medical Journal with an English version - it was translated also into many other languages [5]. Kielholz examined ambulatory patients, whom he saw, and I assessed those who were inpatients in the Basel Psychiatric University Hospital, the Friedmatt, where I worked from 1953 to 1967 – with an interruption of one year in 1954/55 which I spent as an assistant physician at the Beilinson Hospital in Tel Aviv. Anyway, we collected the patients. Professor John Eugen Staehelin, our chief, begged us to put our two studies together. Schmidlin also published on the antidepressant effects of Tofranil. This was at the American Psychiatric Association meeting in San Fransisco 1958 [6]. He also published his Index Psychopharmacorum with Poeldinger [7]. Later in 1985, when Poeldinger succeeded Paul Kielholz as one of the Chairmen of Psychiatry and Director of the University Psychiatric Hospital in Basel, he made Kuhn a honorary doctor of the Basel Medical Faculty and he cited Kuhn as the introducer of the antidepressants but he nevertheless quoted Schmidlin's role.

Part of what one hears is that the reason that Geigy and the other companies perhaps had problems trying to discover an antidepressant was that they were too keen to find another Chlorpromazine. Does that make sense?
I think that depression was not in the centre of their attentions. They were too much oriented towards major tranquillizers and I think it was a huge merit of Paul Schmidlin that he thought of depression. But in Basel we had a tradition because Professor John E. Staehelin, who as I said had been Chairman here since 1929, had written about depressions already in 1955 [8]. He and others gave before tinctura pantoponi or opii simplex (2%) to the depressives, which however were not very effective, but nevertheless had a certain antidepressive effect. Perhaps in later times opiates will be again used in the therapy of major depressions to influence positively the endorphine-system, since the danger of dependence in severely depressive people with their incapacity to feel pleasure is not very pronounced.

In your articles you list other things you'd tried - Prostigmine, Panthesine, Rimifon, Reserpine, and Histamine
Yes... but that was already in progress. Kielholz and I for example gave Histamine to schizophrenics and to depressed patients. We did this to patients having Insulin therapy to avoid any unpleasant sensations due to histamine – pruritus, headache, sexual irritation etc. The majority of the schizophrenics showed no positive effect but most of the depressives reacted with a more or less pronounced mood elevation [9]. By the way Kielholz found that in depressives when you give 2 x 50 gm of sugar, that is the trial of Staub and Traugott, you get a curve like in latent diabetes. The second time

the sugar should not elevate high. In depressives, it not only elevates almost as high as the first time but also it has a prolonged rise and decrease. Kielholz was influenced by Staehelin but he was even more interested in depressions and he published a book on depressions [10] which was also well accepted by general practitioners. He thought that the hypophysis is very active in provoking depressions and because of this we gave also preparations of hypophysic hormones.

Can you tell me something about Paul Kielholz's background?
Paul Kielholz was the son of a psychiatrist. His father, Arthur Kielholz, was chief of the Psychiatric Hospital Koenigsfelden of the Canton Aargau in Switzerland. The hospital was in the countryside. Arthur Kielholz was a psychoanalyst. So Kielholz, from a young age, was exposed to psychiatry because he lived in that general environment. Paul Kielholz was in favour of psychoanalysis but not a real friend of it because his father asked him as a child every morning what he has dreamt last night. That meant that he had reservations. He was a good clinician and observer and very much in favour of psychopharmacotherapy, biochemistry and so on but he was more a practitioner and an organizer of research than someone who concentrated on his own research. He made examinations of autonomic reactions, the cold pressure test and other tests, which were worthwhile in practice to evaluate the state of the vegetative nervous system and its possible exhaustion. His later research was linked to WHO. Dr Sartorius knows him very well and appreciates his achievements. His great merit was in organizing psychiatry in Basel and helping internationally to establish the psychiatric classification ICD-9. He had many friends in the United States, like Freedman, Hoch, Kalinowski, Freyhan, and in Canada, Ban, Lehmann and so on.

Everybody was fascinated by him and this was astonishing because he was not a good speaker, especially not in English. He had a strong personality and 1984 he became the President of the CINP, which was founded by the way by Ernst Rothlin, a pharmacologist here in Basel with Sandoz, with other researchers in that field.

Kielholz transformed the Basel University Psychiatric Hospital and made the proposal that the hospital should be separated from the outpatient department because it was impossible to look after the outpatient department which was always situated in the centre of the town from the hospital, even for an organizer as good as he was. So from 1968 to 77, I ran the outpatient department under his directorship. In 1977 we were formally separated from the Psychiatric Hospital and the University Psychiatric Outpatient Department was integrated in the Basel General Hospital (Kantonsspital) .

Can I ask you more about Paul Schmidlin's background?
Schmidlin was born on July 2nd 1917 and died on November 11th 1984. He did his medical training in Basel and then in 1945 joined J R Geigy as one of the first medical doctors in the firm. He was very interested in psychiatry. Paul Schmidlin and a man named P. Weis, also of Geigy, Frédéric Cornu, M.D., from Berne, and Jules Angst, M.D., from the Psychiatric University Hospital "Burghölzli", Zurich, where Manfred Bleuler was the chief, a man named P. Dick, M.D., of Geneva, Walter Poeldinger, M.D., from Wil in the Canton St. Gallen, and I myself created a standardised system to grasp all psychiatric illnesses but especially depression. Schmidlin took the initiative for drawing up the standardized questionnaire for the examination of depressed patients. We had in mind a double registration, i.e. a nosological system on one hand and a

syndromal system on the other hand. This would have allowed us to examine if the nosology used then was based on reliable symptom-groups.

Then we heard that some Germans (D. Bente, M.D., M.P. Engelmeier, M.D., H. Heimann, M.D., K. Heinrich, M.D., H. Helmchen, M.D., H. Hippius, M.D., and W. Schmidt, M.D.) were doing the same thing and we united with them. Afterwards we linked up with Bobon from Belgium and the Austrian P. Berner from Vienna and we created AMDP (Ausschuss für Methodik und Dokumentation in der Psychiatrie) [11]. I was one of the founders. We met each third month in Basel, in Frankfurt or in Mannheim and created this system. But the new system moved away from nosology and was only concerned with syndromatology. In my opinion one of the failings of the modern systems of ICD-10 and DSM-III is that they wanted to create a syndromal system but, when they retained the diagnoses of schizophrenia, mood disorders and personality disorders, for instance, they made compromises with the old nosology.

Also I don't agree that depressions are mainly mood disorders. Mood is concerned secondarily. I gave a lecture in the Max Planck Institute of Munich on the 29th of May 1997 where I argued that the biochemical and molecular biological findings show that it is a central energetic and cognitive disease with – as Holsboer and co-workers from that institute have shown - a disequilibrium of the limbic-hypothalamic-pituitary-adreno-cortical system and secondarily in most of the cases, but not in all, mood is affected. What we call masked depressions seem to be the real depressions, since the mood is not visibly affected. So, I don't understand why we must have in DSM IV and in ICD 10, the term mood disorders. I would have preferred that they would have remained totally syndromal and afterwards would have made in a second part, a nosological approach.

This idea about depression not being a mood disorder may even come back into fashion soon. At the CINP meeting in Melbourne in 1996, Gordon Parker was saying that melancholia is a motor rather than a mood disorder.
That may be too specific. I call it an energetic and cognitive disorder. Motor is only one aspect of this energy issue. There is also an internal energy that goes along with the whole biochemical process. It is if you want the coming of death into life. Melancholia is a part death if you want. It is a terrible state because human beings live in an eternity illusion and depression gives the idea of nearness of death. In our life times we have death always as accompaniment but only in depression it becomes threatening. The motoric aspect seems to me too onesided.

Did Schmidlin approach you and Kielholz to test Imipramine?
Yes, first Kielholz and then myself, yes, I think towards the end of 56.

What did they ask you to look for? Were they asking for you to look at it in people who were depressed or in people with schizophrenia?
In people who were depressed.

Okay. Kuhn says when he gave his first report that it was working in people who were depressed, despite the fact that Paul Schmidlin from the company was interested in the idea, the company weren't interested. He said two things happened to change things. One was the fact that you and Kielholz also agreed

after you had been asked to try it out in people who were depressed that it did work for depression and the other thing was that Robert Boehringer treated a relative of his with it and they recovered?
Boehringer, yes, was very much linked to Geigy. He was a consultant to Geigy. And it is very possible that he also saw the antidepressive effect but he was also a friend of Paul Schmidlin. Schmidlin was by the way a marvellous imitator of Boehringer, how he spoke and so on. For me it was Schmidlin who had the idea which he got from the protocols of Kuhn in which Kuhn had written thorough descriptions. But Sylvia Schmidlin, his wife, and Schmidlin himself had the idea that Kuhn primarily almost was hindering the progress of Imipramine because he had to be persuaded with all force to continue his clinical trials, when it became clear that it had no neuroleptic, but rather antidepressive potencies.

How did Schmidlin feel then when his role was down-played so much by Kuhn?
He did not like it, but Schmidlin was not a man to defend himself, not at all. Kuhn went on his honeymoon to San Francisco in 1958. He went with Schmidlin and his wife, with Himwich and with someone else, perhaps Freyhan. The American Psychiatric Association Meeting was on there – Schmidlin also gave a paper there - and afterwards they went and gave talks in many psychiatric hospitals, for instance in Denver. Kuhn never mentioned Schmidlin, never. Even in his presence, he never mentioned him. This was in contrast to Kielholz and Freyhan and others. That was hurtful to Schmidlin.

But equally the other way around, something funny happened. When the first CINP meeting 1958 happened in Rome, there were four papers on Imipramine. There was yours, Freyhan and two others but not Kuhn. Why wasn't Kuhn talking?
I have no idea. That is strange. In 58 we were many in Rome – among many others Kielholz, Hippius, Schmidlin, Weis and I myself, all with our spouses. Staehelin did not go. I cannot remember Kuhn there. My speculation is that he was not encouraged by the company. But, Kielholz and I did not need to be encouraged because we were very enthusiastic to publish on Imipramine [12]. So we were sure that we went. I personally went with my wife, along with Schmidlin and his wife and with Dr Himwich. We went by Schmidlin's car slowly to Rome, passing for example one night in Bologna.

Okay. So, was it because Kuhn was obscure in a sense. He was working in an out-of-the-way place.
No. You see in Switzerland these countryside hospitals have an important role. Rorschach for example located also in the country - in Herisau, Appenzell a.R. - but nevertheless, he played an important role. But Kuhn is a special personality. He was philosophically an existentialist who, as he says, was befriended with the great psychiatrist and existential psychoanalyst Ludwig Binswanger. And he was then not chief, only Oberarzt (head physician) of the hospital Muensterlingen of the Canton Thurgau. Zolliker was the Chief. He did a marvellous piece of work on pedigrees - genealogic studies of manic-depressives, it is one of the best archives. Kuhn had a mixed reputation in Switzerland.

Why was there no Nobel prize for the discovery of the antidepressants?
Where the Nobel prize is concerned I have been following this for a long time. There

must be a pressure group advocating it apart from the remarkable performance. Kuhn has almost no real friends but in addition he sees only his own contribution - I am astonished that he mentioned about Kielholz and myself to you - and this may have hindered the recognition of his role.

But he must have a certain merit though because he would say he also discovered Maprotiline and two discoveries is exceptional.
I have no idea if that is true. I know that Keilholz did a lot with this compound but I have no idea who was first in discovering its antidepressive activity. But Kuhn and his wife, V. Kuhn-Gebhardt had another merit about which he did not speak to you perhaps. They treated children with Imipramine for their depression. That is a real merit - that they explored this possibility. They have put an enormous weight on the fact that depressions may begin very early and she has written in a very competent way about childhood depressions. This was already in the late 50s - early 60s.

Let me take you back to 56. Geigy gave you Imipramine to try out in people who were depressed, what did you think of this new drug?
We tried it in a range of people we thought it might help. We saw first that it has side effects, tachycardia, for example, orthostatic hypotension, tremor and we lost also people - there were two suicides. Kielholz and I had a life long discussion about this question of suicide. I said to him in the beginning that the antidepressants have fast effects on activity, that there is no antidepressant and especially not Imipramine which does not have some effect on activity. They can be sedating or activating but mood elevation, I said to him, is secondary. He did not agree. All of a sudden, after many years, he said I think you are right too. I published this view in a paper on Desmethylimipramine in 1963 [13] - the idea that there exists no drug which has a primary effect on the mood. Most of the people felt a little sedated, some were activated but nobody showed no effects in this respect.

Now many authors had already paid attention to levels of activity in respect to suicide. They had written that at the beginning and the end of a depression people commit suicide because their energy has returned or is still present. That is right but I discovered something additional. When the mood begins to improve after the energy, then people feel sometimes more depressive than in the deepest depression because in the most deep depression they are often not even able to feel and it is only after their energy returns, at the beginning of recovery, that the whole misery of feeling also returns and makes them suicidal.

Okay, so you were impressed by the side effects of Imipramine. What though did you see as the therapeutic effects?
You see this energizing or sedating effect could have a therapeutic value or could have a very dangerous value. But when a patient says at the beginning of the treatment he feels only these side effects, I say this is a good sign. It acts, let us wait. Second, the opinion that all antidepressives show activity only after 8-10 days is not true. The SSRIs for example can show their energizing activity already after 24 hours. The patients then don't feel in general very much but the doctors should see it.

I think that the antidepressants are like buckshot on a system which is very differentiated and we influence many transmitter systems and ligands and receptors

and so on. We are still in the beginning of research. We need more specific drugs but that will be very difficult because there are so many processes in our brain which are all interlinked and involved in the process of depression and this makes understanding very difficult. Furthermore there is the blood-brain barrier, which hinders some compounds to be active in the brain.

When you began to give Imipramine first, you were being asked "is this an antidepressant". When did you begin to say yes it is, how many patients did it take?
I think after we had treated approximately a hundred patients we said it is an antidepressant, yes.

There seems to have been some question then in the Company as to how big a market there might be for this kind of compound. At the time it seemed, which is hard to believe now, that people felt that there weren't very many people who were depressed.
Unbelievable because at least in our hospital in Basel, Staehelin and Kielholz spoke always of the many depressions. It was also unbelieveable because Carl Koechlin, who was the President of Geigy company, came from an old Basel family and he should have known that depressions are frequent because many of the old Basel families have a tendency to depressive moods. But you see people from old Basel families, just like Professor Staehelin who was linked also with Koechlin, are always reluctant. It is an old Basel character and tradition to be more than prudent. Geigy were more successful than Ciba in the realm of psychopharmacology. But even so they had to be persuaded and there Boehringer played an enormous role. I can imagine that this reluctance as I said comes at least partly out of the Basel character. On the one hand, they are very innovative but on the other hand they have to be really persuaded until they introduce a drug.

We have now changed to the point where the WHO estimate is that on any one day there are 100 million people in the world who are depressed. Now it seems to me that something extraordinary has happened from the mid 1950s when it was thought that depressive diseases were relatively rare to now when they are seemingly so common. Paul Kielholz seemed to have a role in that as well in that the set up the Committee for the Prevention and Treatment of Depression.
In the beginning of the twentieth century the attention was not on the depression. It shifted to it after World War II. But the statistics show preponderantly the attention that the populations and administrations take towards an illness. Kielholz was always of the opinion that the major depressions remained constant over all time since they are preponderantly hereditary diseases. What increased are the depressions resulting from a more and more stressful human environment. Also the demands of the norm oriented modern society puts more people into a situation of not being able to cope. This explains partly the increase but the statistically shown increase is partly also due to the attention being paid to the phenomenon.

Fine but on the score, part of the reason for the increase, is surely because people like Geigy and Paul Kielholz began to encourage people to recognize and treat depression. Where did the idea come from...
Kielholz has written a thesis on this area for his senior lectureship. He was interested

in the question of depression and people like him taught general practitioners to see it. This meant that people were more sensitive to detect it. That is true. But you want to know why and how it began.

Well partly what I am asking is this - was the group that was formed here, the International Committee for Prevention and Treatment of Depressive Illness, the first group of its kind?
I think so. Paul Kielholz and B.G. Cassano, Italy, were the initiators but also Alfred Freedman and Fritz Freyhan from the United States, C. Fazio from Italy, Hanns Hippius from Germany, Pierre Pichot from France, Stefanis from Greece, Norman Sartorius from WHO in Geneva, and many others. It was founded 1975 in Rome at the International Congress for Psychosomatic Medicine. That was the force of Kielholz. He had, as I said, a strong personality - in spite of having difficulties to speak well grammatically. He could convince people and had a good radiation. He was generally admired in any group. The general practitioners of whole of Switzerland and indeed of the whole of Europe appreciated Kielholz and his scheme of the different antidepressants. He had a huge influence on European and even international psychiatry.

Where did the famous scheme about different antidepressants acting in different ways to get depressed patients well come from?
I think that Paul Kielholz was also influenced by our discussions during many years when he made his scheme. In the paper I mentioned on desmethylimipramine, which compared the results of seven psychiatric centers of Switzerland and Germany, I wrote something which is still true now, namely that at this point in time we cannot separate the antidepressive effect from the positive or negative effect on activity. From that point of view, a drug like Desipramine was extremely important because it seemed to be more activity enhancing than others. It activated people but it had not the same secondary mood-elevating effect on as many depressions as Imipramine. It was less effective, but it had a good activating effect.

Okay. Let me take you to the neuroleptics. You've described a neuroleptic withdrawal syndrome. When did you start thinking that this might happen?
I discovered all this in the course of a research program first of all in 1963 - when I stopped in 81 patients all of a sudden neuroleptics they had received over months or years. In 1966, at the Vth CINP-Meeting in Washington, I described these effects of this withdrawal and published about it in the same year in "Comprehensive Psychiatry" [14] and in the German journal "Der Nervenarzt" [15]. These papers give details of a study that I am not sure that I would do today or if it would be allowed ethically to do it now. We withdrew neuroleptics of all different kinds and antiparkinsonian medicaments and I saw that out of 81 subjects, 55 had withdrawal symptoms. Significant results came out when an antiparkinsonian drug like Biperiden was also withdrawn, but when the neuroleptics alone were withdrawn there was a clear trend. The figures pointed strongly to a drug-dependence of a non-addictive type. At the CINP, especially with Abe Wikler from Lexington, we discussed this at length and I said that WHO had to introduce an 8th type of drug dependence, one without addictive capacity. It was a very interesting debate. To the present day I am of the opinion that there are drug dependencies which have nothing to do with an addiction. We could even say that each drug which acts on the brain causes more or

less a dependency but this need not necessarily be addictive.

Now this has never been widely accepted.
It has been accepted by the CINP in 1966, but it has not gained a wider attention. This was partly perhaps also because of myself since I was never interested to put my name forward. I was always interested in new domains and I am also from Basel, so it is not my affair to put my name always first. Secondly, drug dependence was so widely accepted as addictive. Because of that this was considered as unimportant, even though I think that everybody would accept the idea in theory.

I certainly have a few people who have been under neuroleptics for 10/20 years and there are particular people for instance who because they were given the combination Parstelin accidentally got a neuroleptic and then when you try to change the antidepressant, even if you change them to Parnate, so that they are on Tranylcypromine still, they have awful problems. Now I don't know how long that syndrome goes on for ..
I do not know how long the withdrawal symptoms would have lasted. I had to stop most of them after 24 hours to 5 days because the patients suffered too much. Only with two patients could I wait until the withdrawal symptoms disappeared after 1 or 2 months. I had 11 who had severe neurological symptoms. One patient had all of a sudden torticollis spasticus and - it was during the night - I had to run to the hospital, out of the bath I was in, and I said why do you wait - give the old drug again - Chlorpromazine, and the symptoms disappeared within minutes. These phenomena could go on longer - even lifelong in the form of tardive dyskinesia. Today we have the possibility to give Clozapine, which sometimes works in dyskinesia. But I saw that with the withdrawal of neuroleptics tardive dyskinesia might emerge for the first time.

Tardive dyskinesia is, in one sense, very obviously a withdrawal effect. Could there be something similar in the vegetative system, a vegetative instability that happens, an affective instability, after the drugs are halted.
You see it is a very complicated rebound of many many processes. Only 11 of the 81 we studied had neurological problems but 10 suffered from nausea and vomiting, 7 from oral dyskinesia, 13 from problems of circulation etc. This shows me that it must be a hypothalamic-diencephalic disregulation of some sort but we don't know all the components that participate in this. Neither do we know exactly what is in other abstinence syndromes. I think that it is important that people know about this type of withdrawal symptoms - it has a significance for both hospital and outpatient psychiary.

You have made a number of significant contributions but yet it seems to me that you are not as widely known in psychopharmacology circles as might have been expected.
I was approached by Tom Ban recently who said in the beginning I was very active in psychopharmacology but then dropped out. This is not totally true. I was involved in all realms of psychiatry, psychotherapy, including group psychotherapy, suicidology, social psychiatry, theory of the hunger diseases, the aggressions etc. and last but not least in psychopharmacology. I was also involved when they wanted to ban Clozapine in the seventies. I don't remember in which CINP meeting it was but I gathered some Americans and I proposed that we tell Sandoz that we would sue them if they remove Clozapine. We all agreed that we would sue them. After I had published together with

co-workers a paper on Clozapine in 1977 in Comprehensive Psychiatry I got from Sandoz a grant in 1992 to examine the results of the long-term treatment with Clozapine. This led to papers which I have published together with co-workers at the CINP-Meeting in Melbourne in 1994, and 1997. So I was involved at the start of psychopharmacology but while I was not as active in this field later, I didn't drop out.

To come back to the discussion over the antidepressants. I knew Sartorius through Kielholz a long time. I went also when Kielholz organized meetings on depressions here and met him sometimes at these occasions. At these meetings it was often asked what does Dr Battegay think about this. When I saw that they asked me so often, I didn't want to provoke problems with Kielholz and so I retired from the area although I have quietly written a book on depression [16]. You see Kielholz told me always, that I had a gift for this area. I said to him "I have a solid trouser to sit on and to work". We were always friends but nevertheless there was a latent rivalry problem. Because of that although I was very sympathetic to Sartorious, I retired from official meetings in the realm of depressions. I wanted that Kielholz had his area which was psychopharmacology - that left me the rest of psychiatry if you want. That was good I think for the whole movement. For me it was not even sad. I had all the attention I needed with my research and many books and papers on group psychotherapy, hunger diseases, depression, anxiety, aggression, autodestruction and the addictions etc. But, this affected the recognition of the withdrawal-symptoms of neuroleptics for instance. There were others like Degkwitz from Freiburg in Germany who described relatively early tardive dyskinesia but did not see that it also comes with withdrawal. That was really my achievement. But even now I am ambivalent to underline it. You see it is the Basel spirit. Even my assistants here don't know that I had a part in this story.

I have two or three women who seem to be having an on-going syndrome without neurological problems. It's more a hypothalamic syndrome it seems, what would you do?
You can give Clozapine. It is mostly very effective in on-going symptoms of tardive dyskinesia.

Clozapine seems to have its own withdrawal syndrome though.
You see I am not sure what are the withdrawal symptoms of Clozapine. It must be the case that it has them, but the syndrome seems not to be so distinct as in the others. The problem is much more distinct with the phenothiazines or butyrophenones than with Clozapine. Why I have no idea. But no drug which acts on the central nervous system is thinkable without withdrawal symptoms, when you stop it.

In 58 now, Geigy had their antidepressant but they were still not sure that there's a big market for it, because what happens next, as I understand it is, that they clorinate Imipramine in 58 to produce Clomipramine and they gave it to Walter Poeldinger to try first..
They gave it also to me. And I gave it to one of my assistants named Brandner, I gave it to examine it and he has written about it.

But they asked, it seems in the first instance, at least in 58, they asked for it to be used first in people who had schizophrenia.

No, I tried it in depressives and Brandner seemed to prove that it is not so effective as Imipramine in people who were depressed. It did not work in schizophrenia with this drug, not at all. Only on depressives.

What's this about Clomipramine not being as good as Imipramine.
I thought this after Brandner made his study. But afterwards that proved to be an uncritical view. I think in some patients it is more active than Imipramine and has a more activating effect. And in obsessive-compulsive disorders, in spite of the fact that I am of the opinion that the producers exaggerate in stressing the anti-compulsive effects, I accept that it has a certain effect. Perhaps in elevating secondarily the mood, the compulsive tendencies can be more or less neglected.

Walter Poeldinger, I think, when he tried it was asked to use it first in people with schizophrenia.
Perhaps. But he was not in Basel then, he was in St Urban, Canton Lucerne. Poeldinger, coming from Vienna, was first involved in psychiatric hospitals in the countryside of Switzerland and he tried many many drugs. He later came as head physician to Basel, became here senior lecturer, left then again and went again to Vienna but later came back and lastly in 1985 was elected as Professor of Psychiatry and Director of the University Psychiatric Hospital in Basel. He was very active in using psychotropic drugs.

Who was he, what was his background?
He was born near Vienna. He was the son of an employee of the state railway, I think, and was found to be intelligent enough to study. He studied medicine and was impressed by the psychiatry of Professor Hans Hoff in Vienna. Hoff was an extremely intelligent but also a very authoritarian man. It was told ironically that he shouted for example: "I define what schizophrenia is". Poeldinger came then to St Urban Clinic of the Canton Lucerne near Berne. It was in an old monastery - it was marvellous to see the church there. While he was there he published very actively. Kielholz took him then as head physician and he was also very active here. He became the leading doctor of the depression ward which Kielholz had formed. Then he returned to Vienna. Later he returned to Switzerland and was Co-Director of the Psychiatric Hospital Wil in the Canton St. Gall. When Kielholz retired in 85 the question came up as to who would be his successor. We had difficulties to chose. As a compromise I proposed Poeldinger and he was chosen in 85. Until 94 he was here. He remained very aware of the new psychopharmacological developments but was not so much interested in leading his hospital. He has written among many other papers and books, together with P. Schmidlin, the "Index Psychopharmacorum" which appeared in repeated editions and serves as a very valuable overview on psychopharmacology.

What are his merits? He continued the interests of Kielholz. He always was aware of the new research developments but Kielholz was much more effective as the director of a university hospital. Poeldinger was perhaps hyperactive also in visiting many congresses, that was his character. He was interested in all domains of cultural life too. He knows very much and is a very nice personality. But he was not a person like Kielholz who could push something through by keeping steadily at the matter. He was a good follower but not an initiator.

Did you get to use G22150, the precursor of Tofranil.
I don't remember but we had also had other drugs... in the fifties we had from Sandoz a precurser of Thioridazine, NP207. It had marvellous effects on paranoid schizophrenia but after some months we saw pictures like retinitis pigmentosa and the patients could no longer differentiate colours so well. A terrible problem so we had to suspend treatment. The patients began again to see colours later but the retinitis picture remained. So we had also some trouble. With chlorpromazine, by the way, we had also one death in a patient who symbollically knew about her death. Professor Staehelin was reluctant to begin the chlorpromazine therapy with her but we, the young assistants, said, we begin. An old female Israeli psychologist said she would die but the patient seemed to be somatically healthy - we examined her and so did physicians who were internationally renowned and nothing was found. But after some days she was dead in the bed from a fulminant lung-embolism.

Fascinating.
Her prophetic visions were fascinating. I got requests from Jungians all over the world for reprints of my paper "Prophetic Statements in Visions and Dreams of a Schizophrenic Woman", which appeared 1960 in German in the "Swiss Archives of Neurology, Neurosurgery and Psychiatry" [17]. She identified with Christ and felt like him cruxified. And marvellously she saw first the open sea and on it Maria the mother of God. Then she saw a cross, but not so long. She said that she knew that it was a sign of God for a change and she prayed for all mankind. In one of her other visions she saw again "a huge, terrible water, a sea, then a house, which was overflown by the water".

Did you know Jacob Klaesi.
Klaesi was the founder of this outpatient department in 1923. He was head physician of the hospital and had at first at three afternoons a week to receive psychiatric patients in a room of the University Medical Outpatient Department. I knew Klaesi in his late years - he reached the age of 98. He told me "I am very unhappy that I am known for the sleeping cure", "I am the first" he emphasized, "to have introduced short-term psychotherapy". Then he said: "I want to tell you a small story: A woman with a fine figure, a noble woman from another country, came to me and I said to her 'why do you wear such a terrible hat'? She said "I thought that I came to a doctor not to a butcher". He answered "No I am very astonished, shocked, you are a fine lady and what is this". Then she told him that her husband was never giving her attention. He pretended in four sessions he healed her. He wanted to be recognized because of this short term psychotherapy and not because of the sleeping cure.

When he talks about the sleeping cure he talks about it as a means to open people up for psychotherapy.
That is true but I think he introduced that when he was in Burghölzli in 1917 but here he founded the University Psychiatric Outpatient Clinic - naturally on the initiative of the authorities and of his chief, then Professor G. Wolff M.D., who was the chief of the Basel University Psychiatric Hospital and also a doctor of natural sciences.

What about this idea that one of the things the physical treatments do is to open people up for psychotherapy of some sort or another.
Yes, I agree, but I am also of the opinion that psychotherapy is at the same time a

physical treatment, since it acts via organs of sense on the brain, and that the physical treatment is also a psychotherapeutic one. I don't make the separation of mind and body. If, for example, we speak together we hear and see each other and this means a somatic process goes on which at the same time is an experience. In German there is a much better word than in English for that - "Wie er leibt und lebt". We could translate this saying: "As he bodily exists and lives". But in principle you cannot translate the general phrase. The German language knows that the somatic life at the same time is psychological experience. When I do psychotherapy, then you could measure the ongoing somatic parameters. Psychotherapy is in that sense not a psychotherapy but a holistic therapy which must in the same manner as medicaments influence the somatic processes. Aaron Beck, from the United States, who created cognitive therapy saw that with this cognitive-behavioural therapy, he can influence in the same way as the pills depressed patients. Adding Amitriptyline gave no different results.

Roche was almost to going to support me in the project on a comparative investigation on cognitive-behavioural psychotherapy on one hand and Moclobemide on the other hand, which I had planned to do together with Isaac Marks in London. But apparently they feared that psychotherapy would have the same effect as the drug. Roche's decision seemed to me not wise. Even if psychotherapy would have the same effect, many people would prefer to take Moclobemide than psychotherapy because psychotherapy needs an own effort.

Do you not think that we tend to just give pills rather than do therapy and the culture of pills becomes almost anti-therapeutic - you give a pill and you don't look at the person's whole situation.
That is a danger, but you could even in some very severely disturbed, for instance, just put the pills on the table, and go out and it would still have this energizing or antipsychotic effect, supposed they would take it. But man wants to be always accepted as an experiencing human being - he wants always to be taken seriously and to receive full attention.

I don't know Dr Healy if psychiatry is really necessary, since each doctor should know about the necessity of a psychologically adequate approach to the patient. But if there were no psychiatry, perhaps nobody would care for this empathic and holistic approach which is very necessary I think. I think that in psychotherapy the technique is not at all important. Studies were made of this. The outcomes depend on the personality and the pattern of approach of the therapist. As Lieberman and coworkers showed in 1973, which has since been confirmed, if you are a provider and/or an energizer, you have success. The laisser-faire-type achieves no good results. But, I have very often major depressives and after I have spoken with them and they with me, they seem to be rid of their depression but it comes back when they are leaving after a few hours. So, if you do psychotherapy as monotherapy with these patients it is, therefore, difficult. You should combine it with antidepressants and you have to give them your phone number. They can often only promise for a day that they don't suicide. Ambulatory treatment, which we prefer today, is linked with a certain risk. Today we give psychotherapy together with antidepressive drugs because it is unethical to let them suffer, even an hour or two too long. But, as I underlined, the somatotherapy is always also psychotherapy, especially when the psychiatrist or other doctor has the necessary

empathy for the patient.

In your 58 article on Imipramine, it's not clear what you think Imipramine is working on, you say that it's not shortening the phase of a depressive illness and you also open up the possibility that it might be acting on something temperamental rather than on an illness.
Kielholz and I have written that under Imipramine some patients show already after 3 to 10 days an activation and an opening for the environment and shortly after that a mood elevation. We differentiated from those patients who reacted only after 10 to 21 days. With antidepressants I have, however, in single patients also observed a reaction, who say yes, I am less depressive, but now I do not take problems so seriously. When I tell them that this is very good, they say ”no, now I have no longer the personality I had before. I cannot continue to take these medications. It makes too huge a distance between the problems and myself at this point”.

This is a kind of derealisation ?
A loss of the desired link to outside reality. It's not a derealisation but they seem to experience a filter between them and reality.

But I have written also about the effect of the psychotropic drugs on the hospitals. The psychotropic drugs, especially the neuroleptics, meant that the walls could be taken away. They meant that the communicative capacities of the schizophrenics were discovered. This changed totally the existence of the schizophrenics and it meant that others saw that they were human beings. In 1953 when I began training, I took over among others, a department with chronically ill schizophrenics and I spoke with all of them. One of the head nurses told me don't you know that it is not allowed to speak with schizophrenics - otherwise you irritate them. I said don't you think it is a good thing to activate them, they are human beings. You are perhaps pleased that they are silent but I am pleased when they are active. He couldn’t understand.

I think that these neuroleptics made psychotherapy possible with schizohprenics. We have in Basel also Professor Gaetano Benedetti, a world renowned psychotherapist of schizophrenics. He agreed that the neuroleptics facilitated the psychotherapeutic contact with schizophrenics. I developed group psychotherapy for these patients and I think it is even a very great mistake not to take schizophrenics in therapy groups because I think that the group settings facilitates the schizophrenics to enter into communication with others and to take their drugs because they see when others in the group omit to take their drugs how they then relapse into delusional states, irritations and aggressions. Tienari in Finland and other authors reported about the same findings.

I should ask you about Ernst Rothlin, what was he like.
Rothlin was a very intelligent man. He was a Director at Sandoz and was very important there in developing psychotropic drugs and studying brain processes. But when he approached the age of seventy he came back once from vacation and saw that his office was occupied with another man. He had to retire and founded with other researchers in psychopharmacology the CINP which had a big success. He was an authoritarian man but he had good radiation and could convince many others for his purpose. I knew him more when he was an old man and had grown to wisdom. So, it is

difficult to know if all my judgements will be right.

When you gave Imipramine first and when Kuhn did too, it was intravenous and Kuhn reports in the first few people who got all seemed to respond within a week.
We at first never gave it intravenously, but intramuscularly. And I think Kuhn also gave it intramuscularly, first 25 mg and then we increased. Intravenous infusions came only in the early 70s.

Do you think there is a difference between either the intramuscular and intravenous preparations and the oral preparations.
We thought, and I think our thought was right, that it is active sooner when given intramuscularly instead of orally and even more so when given intravenously. With Anafranil, when I gave it intravenously, after 24 hours I saw in some patients already a difference.

When did you become aware of Anafranil's OCD effects.
I think only one or two years after Clomipramine had been marketed - not at the preliminary stage of trial. That was not my spontaneous discovery, I only became aware of it after it was pointed out to me.

Who do you think did pick up the anti-obsessive compulsive effects, who were you aware of beginning to talk about it.
Well F. Freyhan [18] was always pointing to the fact of the importance of target symptoms in psychopharmacotherapy but in 1960 after his idea came out, and later, we were all seeking for targets so I think we were all sensitised to this issue. Freyhan was a very well educated man who had a huge knowledge not only about psychiatry, but also about philosophy. His mother was, by the way, a relative of the great psychiatrist and philosopher Karl Jaspers, who was University Professor in Basel since 1948, where he lived until his death in 1969.

Can you tell me more about the target symptom idea. Where did he get that from? Was it all his own?
Freyhan had the idea after the introduction of antidepressive drugs. With Imipramine he thought that the mood was the main target symptom. He sought a target symptom for each drug. He thought the diagnosis is important for the course of the disease, but the target symptoms are decisive for a pharmacotherapeutic influence. The course of the disease is important for how long you should give the drug - whether it is recurring. I agree with him totally that the symptoms are decisive for the choice of the treatment. When, however, DSM IV or ICD 10 speak of delusional states (of a non-schizophrenic type) I have to say that there are different paranoid syndromes which are not schizophrenic and therefore cannot be treated in the same way. One was described by Emil Kraepelin as paranoia and later also by Ernst Kretschmer, which comes following a life event, which may be totally unimportant for someone else but is a narcissistically injuring key event for this person and it leads on to delusional ideas which may lead to dangerous aggressions towards people by whom they feel persecuted. The German poet Heinrich Kleist has written a story about Michael Kohlhaas, in which he describes a man who mobilizes an army to fight for his right against his "persecutors".

Can I ask you about one more state you don't find in DSM IV and we have never had it in the UK but you have had it here, vegetative dystonia.
This was described by Gustav von Bergman, Munich, a physician who was a Professor of Internal Medicine in Berlin. He has written in this context also about "vegetatively stigmatised" people. In the late 40s he has written together with other German und Swiss professors of Internal medicine like Herbert Schwiegk and Arthur Jores a textbook of two volumes, in which he spoke also of a lability of the vegetative system.

"Vegetative dystonia" is a very vague expression. If somebody for example suffered from vegetative symptoms in a state of exhaustion or after a cold it was also diagnosed as this. Many different causes were said to trigger vegetative dystonia. Furthermore it is not clearly distinguished from the term "neurasthenia". Because of these difficulties it is not easy to come up with a clear picture for "vegetative dystonia".

But the interesting thing here as well is that there has been an interaction in that you've had a treatment for it here which we haven't had.
Yes we gave often Bellergal, a mixture of ergotamine, entire belladonna-alcaloids and phenobarbital.

You had Opipramol (Insidon) as well, which we didn't.
Opipramol has according to my experience neither a significant effect on vegetative lability nor on depressed mood as was primarlily presented in the advertisements. I stopped using this drug many years ago. As I already said, I do not like this term, vegetative dystonia. It is not clear. And so many people would have at least in certain conditions a vegetative dystonia that you would have to give a treatment to the whole people - for example after passing a night without sleep, many persons have a vegetative dystonia. In Switzerland concerning psychiatric therapies we are pragmatic. Eugen Bleuler helped to introduce psychoanalysis here but also somatic treatments. And we did not stick with psychoanalysis, we welcomed all other psychotherapeutic schools, and we tried the different drugs when they came on the market. Perhaps this is because in Switzerland we are forced to live together with 26 Cantons and not only the Cantons but each community has its special traditions and special dialect and we are always forced anew to learn by trial and error and to watch critically the results of our decisions. When a system approaches, like the European community, we fear because we try to let everybody live according to his or her philosophy, as long as it is a democratic one. But we do not want to be dependant on a foreign capital, far from our country. In the modern world this suspicion against a larger body represents a huge problem and with time will have to be overcome.

You mentioned Moclobemide earlier, can I ask you about social phobia which has the makings of a modern epidemic?
I think in former times we spoke more of shyness. Shyness can be a normal phenomenon or the most pathological. When it is hindering a life, then you have to act. Now psychotherapy needs a lot of time, so if you can alleviate the life of these persons by a drug, why should you not do it. Social phobia can for example be a sign of a neurosis or a sign of the beginning of a psychosis or of a depression or even of the beginning of organic brain disease. You see we have only approximately 10-12 syndromes in psychiatry. It's a very easy branch of medicine you could say but these syndromes can be provoked by different means. Social phobia is one of the syndromes

but it is not a basic syndrome. It is mostly linked with others and represents often a co-morbidity.

My interest in social phobia is that while there are fairly severe forms that have to be treated, it is also possible to over-medicalise what is a normal variation? Absolutely. And a certain shyness may be worthwhile. I don't like disinhibited persons, of whom I know already very soon all that they have to say.

But in the case of social phobia are in the industry trying to sell phobia now in order to sell Moclobemide for instance in a manner they once sold depression. That's it. Its very similar. But social phobia has not the same significance as depression. It is mostly a part and often not the most important syndrome whereas depressions are profound disorders, psychophysical processes which because of the suffering they include, have a huge significance.

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