The Introduction of Chlorpromazine to North America

Excerpts from a talk given by Dr. Heinz Lehman at
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I thought I should perhaps give some sort of a feel what things were like in the 1950s, just immediately preceding and immediately following the discovery and introduction of the psychotropic drugs. I was working at the Douglas Hospital in Montreal. It was a small hospital - not small in the number of patients, we had some 1500 or 1600 - but we had very few physicians and very few nurses, one registered nurse for 600 or 700 male patients; the others were all untrained personnel.

It was pretty horrible to work under those conditions: I felt the only way to keep morale up in the 1940s with the few doctors we had then - most had gone to war - was to do some sort of research. So I did all kinds of things, always convinced that psychotic conditions and the major affective disorders differed in principle from neurotic and personality disorders, and they, I was convinced had some sort of a biological substrate. So I kept experimenting with all kinds of drugs, for instance, large doses, very large doses of caffeine, I remember, in one or two stuporous catatonic schizophrenics - of course, with no results… We experimented with an extract of the pituitary gland, which we thought might have some effect on psychiatric conditions. So I gave it to some of my schizophrenic patients. We kept good records of our patients then - actually daily progress notes - and there was suddenly, on October 16, you see a very long note, describing a miraculous, very dramatic improvement, almost overnight, from one day to the next: the patient was lucid, cooperative, rational, he had a different posture - it was dramatic. Word associations were a more objective marker, I thought, than just recorded observation~; I always had a stop watch when I made rounds, and I took on various days this patient's association times. On the first two days association times were all over the place - 70 seconds, 15 seconds, 80 seconds, and so. But on October 16, 1939 - that was the day when the patient was so dramatically improved - they were quite within the normal range. So we had great hopes for this "extract 47," until we found out, within a week or so, what had really happened: this extract had a high alcohol content! It just shows you that even with the best efforts and looking at all kinds of different criteria, whether they are rating scales or other criteria, one has to be very skeptical, before one accepts even dramatic results as being promising or novel treatments.

We did all kinds of other things. I injected sulphur in oil which was painful and caused a fever; I injected typhoid antitoxin intravenously which produced pyrexia in schizophrenic patients. Nothing helped; I even injected turpentine into the abdominal muscles which produced - and was supposed to produce - a huge sterile abscess and marked leucocytosis. Of course, that abscess had to be opened in the operating room 'under sterile conditions. None of this had any effects, but all of this had been proposed in, mostly, European work as being of help in schizophrenia. The best results I could obtain were with prolonged sleep, which Klaesi had introduced in the 1920s, but that was quite a dangerous procedure, because it often led to pneumonia and we did not have penicillin in those days. All this led to a lot of frustration but no discouragement. I kept on looking for something. We had of course insulin-coma treatment and we had electro- convulsive treatment. Electro-convulsive treatment was very dramatic, the patient was symptom-free

within a week, but two weeks later he had all the symptoms back again. With insulin coma the trouble was that you could treat only about 10 or 12 patients at one time; it was very expensive. The patient sometimes occupied a bed and several nurses for 3 to 4 months; so with the many schizophrenic patients we admitted, it hardly made an impact. And after the patient left the hospital - if he was better after 3 or 4 months of treatment - we knew that 7 or 8 out of 10 patients would come back within a year, and the next insulin coma treatment usually was not so successful.

There was a need for a real breakthrough, and that came. One day, and this will sound familiar to you, there was a detail man from a pharmaceutical company - as it happened he came from Rhone-Poulenc - and he left all kinds of literature and samples. My secretary told him that I was much too busy to see him, but he said: "It isn't necessary, I'll leave this here, this is something new and so good I don't have to explain it to him, he will certainly pay attention to it once he reads it." Now, I thought that was rather arrogant, but it caught my attention, and the next Sunday, in the bathtub where I do much of my reading, I read 3 or 4 of Dr. Deniker's papers on chlorpromazine. When I read about the new French drug, I thought it was just another non-barbiturate sedative. But there was a certain statement: it acted "like a chemical lobotomy," which puzzled me, and I said to myself, there is something more to it. Obviously these two, Delay and Deniker, are very sophisticated psychiatrists, they must know what they are talking about, they seem to think that it is something very new. What I did then was to convince myself that this really was something different from the usual sedatives such as paraldehyde or the barbiturates or chloral hydrate. To try this, I asked for 3 or 4 volunteers, actually we had about 7 or 8 altogether, among the nurses. In those days research was an exciting word, and people were very anxious to volunteer for it. One day the volunteer nurses were given an oral dose of chlorpromazine, I think it was 50 mg, which made them quite drowsy. And on another day, the next week, they were given a dose of sodium barbital which made them equally drowsy. Now I wanted to see whether there was really a difference in these states of drowsiness. They were both producing quite similar phenomena: their movements, their general appearance, in the way the nurses talked and the way they felt. I gave them performance tests: reaction time, tapping speed, digits forwards and digit substitution - these tests are still being used to test for alertness and vigilance. Now, the volunteer subjects were tested before, and then again after they had become drowsy with the drugs. With sodium barbital, their performance was worse on all tests after than before the drug was given; with chlorpromazine, however, 2 or 3 of these tests were actually performed better when the subjects were in a drugged, drowsy state. Now, that was unheard of, and difficult to conceptualize - at least, I could not at that time. If somebody was drowsy and drugged, he was 'dopey.' Of course, his intellectual functioning and motor performance were impaired; the two could not be dissociated, i.e., performance impairment and drowsiness. But here was proof that the two could be dissociated, and the chlorpromazine apparently affected selectively initiative, alertness and vigilance, but not intellectual and motor performance. That convinced me that here was something unique. The next psychiatric resident I met the following day I asked whether he wanted to work with me on a study, and he said, why not? We got 74 patients - that took us all of a week - and we started giving them chlorpromazine, not sequentially but all simultaneously. That was in May 1953, and by July we had all the results. By August we had written up the paper, and sent it to a journal. It was not published until March 1954, for reasons that are still somewhat obscure. Now, try to realize what had happened: we had no protocol for this; we had no permission from the government to use a new drug (we did not need this at that time); we had no informed consent (the concept of "informed consent" did not exist at that time). The patients and their relatives were

very happy that something was being done for the patients. I did not even have to ask permission from the director of the hospital. I simply did what I thought I should do. So with all this freedom and no protocol, it is no wonder we could do the whole thing with over 70 patients in 3 months. But please, remember also that we got no extra money, we did not even get part-time help of a single secretary or nurse; the whole project had to be folded into the routine work; and then it became very evident that we had something that was indeed unique. When I wrote it up and gave the manuscript to the director of the hospital, he noted that I had used the word "unique." He said: "You never use the word 'unique' in anything that you publish, because you always regret it later on - there is no such thing as 'unique.' Something may be better, or different, but not 'unique." I insisted on 'unique', because it was a good thing, and it was really a unique therapeutic new weapon.

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