Editorial

Are Modern Tranquilizers Addictive?

In 1952 I first heard about a drug from France which had remarkable properties in treating psychotic patients. It had just become available in the United States, a transplant via Canada from Rhone Poulenc of France. The Canadian representative tried to peddle it to United States companies starting from the largest and working his way down to the least significant. He was rejected by all the companies with the exception of the last, a one product company whose medical director had the vision to realize the importance of this product. What was known as Chlorpromazine in Canada became thorazine in the United States. That company today is one of the largest.

We had not yet formulated the adrenochrome hypothesis nor its offshoot, that vitamin B_3 might be therapeutic for schizophrenia but I could not obtain any until the Canadian subsidiary of Rhone Poulenc made it available commercially. Chlorpromazine was the first major tranquilizer, discovered by the French surgeon Henri Laborit, and tested by French psychiatrists. Dr. H. Lehmann in Montreal soon confirmed the European reports as did the medical director of the United States company. They both submitted papers at about the same time. Lehmann reported his clinical observation on about five manic depressive patients and the other physician reported on a much larger series of schizophrenic patients. Lehmann's paper was accepted immediately while the other paper was sent back for some revision. Lehmann became known as the father of the tranquilizers in North America. Chlorpromazine is an anti-histamine. These antihistamines were made in Italy by a chemist Dr. D. Bovet, who received the Noble Prize for his work in chemistry. The first anti histamine is the common drug benadril, now available over the counter. The rest, as is said, is history. The need for this type of drugs was great, the potential for profit was immense and the combination of need and greed soon propelled this and similar drugs onto the market. They were very successful in controlling psychotic behavior. It was assumed that this meant that patients were also recovering from the illness, but from the beginning farsighted psychiatrists realized that patients who took these drugs paid a major price. Dr. A. Meyer-Gross, in the late fifties, author of an impressive text on psychiatry, claimed that these drugs merely converted one psychosis into another.

However, they were necessary. The ill-conceived deinstitutionalization became possible because the drugs cooled the symptoms and made the patients' behavior more tolerable to the community even though they did not get well and began the revolving door process where psychiatric hospitals became first aid stations for refuelling the patients with drugs, much as cars get refuelled at gas stations. The major difference is that cars and the fuel are perfectly adapted and the cars run well. I call the tranquillizers essential evils because they are essential for many during the treatment process and because the consequence of using them alone is so evil in causing side effects and deterioration of life. The first drug, chlorpromazine, marked the new paradigm of treatment using powerful drugs that were not narcotics, but they were not curative and the race was on to find better compounds that would be more effective and less toxic.

This search still continues. The present day drugs are effective with fewer milligrams of chemical per day and they have different side effects, but the efficacy of the new class of drugs is really not much better than the efficacy of the old drugs, Dr. F. Geddes (British Medical Journal 2000; 321: 1371-6) analyzed 52 therapeutic trials involving over 12,600 patients. He found that compared with conventional drugs at a moderate dose, atypical antipsychotics caused fewer side effects but had similar

effect on symptom reduction. The main advantage of the newer atypical drugs was that one had more choice. There will always be patients who do not respond to older drugs who will respond to newer ones and so on. Geddes recommended that the conventional drugs should be used as the initial treatment.

I am not in principle opposed to using drugs especially as part of orthomolecular treatment. In orthomolecular therapy we use the drugs to obtain control of "hot" symptoms of psychosis. By "hot" I mean those symptoms which force patients into hospital or into some other institution like prison. These symptoms include severe psychotic behavior, severe hallucinations, severe depression. For example many years ago a rural family brought their son to me. He had been sick several years but spent most of the time sitting quietly in the kitchen. The family could tolerate this. But one day he began to hop incessantly on one foot. Within a few days the family was exhausted and he was forced into hospital. This was a hot symptom. The cool symptoms may be just as severe but they do not grate on the nerves of a family and society quite as much. They include milder hallucinations, especially if the patient does not talk about them, thought disorder, since most are not aware it is present and moderate depression and states of hypomania. The tranquilizers are excellent for converting hot into cool symptoms but they do not cure patients.

I see patients who do well on chlorpromazine but do very poorly on any of the new drugs. I am very concerned about the increasing number of chronic patients who are tranquilized with the new atypical drugs, who do not get well and I shudder to think what they will be like twenty years from now. Whereas the old drugs such as haldol caused extrapyramidal side effects which were easily controlled by other medication, the newer drugs are less prone to do so but have a major effect on obesity, on disturbance in blood sugar levels and in causing brain damage with long term use. There is one side effect that especially worries me. That is the difficulty in taking patients off the new drugs compared to the conventional ones. In orthomolecular therapy it is always the objective to have patients drug-free without any relapse and with the older drugs this was not very difficult.

As soon as the patient had shown major improvement the amount of medication was slowly decreased. If there were any signs of recurrence of symptoms the dose was increased again for awhile and then the process was repeated until most patients were drug free or needed so little that there were no side effects. The usual response was relief as the drug effect wore away but if the patients still needed the medication it would become more noticeable after one or more weeks. It was never noticeable the first day after the medication was stopped. But with the atypical antipsychotics it has become an enormous problem. For example, with risperdone it is not too difficult to reduce the dose from high levels to more moderate levels but when one gets down to lower levels even a 0.25 mg decrease may cause a surge of symptoms.

These drugs behave as if they were addicting drugs. With the addicting drugs, such as heroin, as soon as the dose is decreased there is a marked relapse. It takes much longer to reduce the medication and when it is down to 3 mg daily I cannot even decrease the dose by more than 0.25 mg. This I never saw with the conventional tranquilizers. The question that puzzles me is whether these drugs also are attracted to the addictive centers in the brain that bind morphine and heroine. Haldol was conceived by splitting the morphine molecule into two and preparing a structure very similar to one of these components. But haldol is not nearly as addicting. The atypical anti-psychotics however do differ

from narcotics because one does not have to increase the dose to maintain the same level of control. If one takes much more than the recommended level there are major major side effects and no increase in therapeutic power. I would not object to these addictive properties if patients on the new atypical psychotics were able to function normally as they can with orthmolecular therapy. But fewer than ten percent of patients on drugs alone are able ever to reach the level of of recovery where they pay income tax on their earnings. I am also very concerned about the long term effects of brain damage which according to some studies becomes progressivly worse with increase in dose and duration of treatment.

–A. Hoffer, M.D., Ph.D., FRCP(C)