Editorial

Atypical Anti-psychotics Create Dependency Disorders

The USA Diagnostic and Statistical Manual (DSM-IV) lists a condition number 2304.90 entitled "Substance Use Disorder." It describes substance dependency as a maladaptive pattern of substance use, leading to clinically significant impairment or distress as manifested by three of seven listed characteristics which occur in any 12 month period. The characteristics relevant to this discussion are:

• Withdrawal.

• Persistent or unsuccessful efforts to cut down or control substance use.

• Important social, occupational or recreational activities are given up or reduced because of substance use.

• Substance use is continued despite knowledge of having persistent and recurrent physical or psychological problems that are likely to have been caused or exacerbated by the substance.

The modern atypical anti-psychotics produce a syndrome which is characterized by these four items out of the seven listed. There is a major difference between the drugs usually listed as causing dependency and the anti-psychotic drugs. The usual definition refers to patients who voluntarily take drugs such as the opiates, or anti-anxiety drugs to excess and become dependent. The anti-psychotic drugs are given as a treatment for psychosis and are taken on the advice of psychiatrists and very often are forced on the patients by social and legal sanctions if they refuse to take them voluntarily. That is why the parenteral drugs have become so popular. Legal pressure is immense and many patients are forced back into hospital when they discontinue their medication. Two thirds of schizophrenic patients re-admitted are non-compliant with using medication. Recently an attempt was made to deal with this problem using compliance therapy. Patients were given five sessions of cognitive therapy, compliance therapy, each lasting 30-60 minutes. The controls received the same amount of non-specific therapy. This double-blind study found that there was no improvement in compliance.[1] The authors did not discuss side effects and toxic reactions as a reason for this massive non-compliance.

A change may occur since the Supreme Court of Canada ordered that drugs may not be forced on patients against their will. Patients can still be forced to remain in hospital even though they can refuse medication. Nothing has changed so far in British Columbia. A middle aged divorced woman I am treating for anxiety and depression (having first seen her many years ago) became temporarily psychotic a few months ago. She was committed to the hospital and placed upon olanzapine, 10 mg daily. This dose caused intolerable side effects. She was willing to take 5 mg, which was more tolerable, but could not get her psychiatrist's consent. She was treated against her will in hospital in spite of the Supreme Court decision and was discharged under the legal threat that if she did not take 10 mg she would be promptly forced back into hospital. She is desperate to get off the medication and will probably discontinue them on her own.

In the past, I have called anti-psychotic drugs addictive but I was wrong. Addictive drugs provide some pleasurable benefit at least at the beginning of the addiction. The opiates relieve pain and anxiety and cause euphoria, which potential addicts enjoy. But after they are addicted they must continue to use these drugs just to avoid the severe withdrawal symptoms if the drug is stopped. The avoidance of pain and suffering creates addictive behaviour in a society which does not permit the use of these drugs. The one exception is methadone used for the treatment of heroine addiction, which is very carefully tolerated. Society allows the replacement of one addiction, heroin, which is socially unacceptable with the other, methadone, which is equally

addictive but with different side effects. The anti-psychotics may be voluntary at least at the beginning but once the dose is established and the side effects appear it becomes very difficult to persuade patients to remain on the medication. The continual use of these drugs is no longer voluntary; it is forced and should be called iatrogenic, caused by doctors, or societogenic, caused by society. Anti-psychotics are not addictive but create dependency, as described by the APA Diagnostic Manual. A few patients do not experience any side effects and with them compliance is no problem.

Withdrawal

I started using anti-psychotic drugs in 1955 and was involved in a study of haldol, one of first two that became available. These drugs were helpful in reducing the intensity and frequency of symptoms and they changed the entire atmosphere of the old mental hospitals. As soon as the patients became better I would gradually decrease the amount of medication. With orthomolecular treatment the efficacy of drugs is enhanced and not as much is needed. There was no problem with this. As a rule the patient felt better as the dose was decreased because the side effects vanished while the therapeutic effect remained. I cannot recall seeing any dramatic immediate withdrawal symptoms. Many patients without consulting me would suddenly stop taking their anti-psychotic drugs. There was no severe withdrawal but if they still needed the drugs, symptoms, which had been suppressed by the medication, gradually returned. The use of the nutrients decreased the tendency for the symptoms to return. My aim was always to decrease the drugs to the lowest possible dose consistent with good health and minimal side effects. If the symptoms recurred in a few weeks or months then the medication was resumed. This is what is taught in therapeutics in medical schools.

After I began to use modern atypical anti-psychotics the situation changed markedly. Most of my patients were referred to me by their family doctors and had already been treated and failed to respond to the medication, otherwise there would be no incentive to refer to me. They were on medication and suffering from the tranquilizer psychosis. I continued the same practice of slowly withdrawing the medication but I soon discovered that I was observing an entirely new phenomenon. If patients suddenly stopped their medication or the decrease in dose was too great there was a marked resurgence of symptoms the next day, something I had not seen with the older anti-psychotics. If my patient on 10 mg of olanzapine was getting on reasonably well but suffering the usual side-effects such as being overly sedate, fatigued, finding it difficult to concentrate and gaining too much weight, I would start to decrease the dose. If I went down to 5 mg they would suffer immediate withdrawal. If I went down to 8 mg it might be tolerable. The same occurs with risperdal. A patient on 15 mg can be decreased to 10 and eventually to 5 but after that I find they have to be decreased by 1 mg per day doses changed every few months. The withdrawal symptoms are severe and debilitating and only the bravest of patients are prepared to face them again. This ensures that patients will not decrease them on their own. It reminds me of morphine, of heroin and the diazepines: when the withdrawal symptoms appear the drug is usually increased again until they come under control, as with heroin and morphine. If the patients can tolerate the withdrawals and if they are on a good orthomolecular program they may be able to tolerate the withdrawal if the decrease is done very carefully. In vivid contrast a schizophrenic patient I have been seeing for 25 years decreased his haldol daily dose from 60 to 50 mg. Three months later he told me had not suffered any withdrawal symptoms. He was very psychotic many years ago, has been improving very slowly and is now almost normal.

Persistent or unsuccessful efforts to cut down or control substance use

Failure to comply is one of the major problems in modern psychiatry. With orthomolecular psychiatry this is seldom a problem because there are so few side effects from the nutritional program. Compliance will always remain a problem until drugs are developed which have as few side effects as vitamins and minerals. The effort to cut down is prevented by the resurgence of the symptoms of the original psychosis and/or by legal sanctions.

Important social, occupational or recreational activities are given up or reduced because of substance use

Few patients can engage in normal activities when they are on full dose antipsychotics. This is one of the aspects of the tranquilizer psychosis described below. Many years ago a report appeared on the outcome of treatment of 42 schizophrenic physicians. All were treated with the older tranquilizers. After treatment only 12 were able to resume their medical practices and of these 12 six were able to do so because their wives, nurses, ran the office for them and the doctor signed the prescriptions. In sharp contrast I know of 17 young men who became schizophrenic in their teens. They recovered on orthomolecular treatment. They then became doctors. Three of them achieved very prominent positions. One is Chair, Department of Psychiatry at a major university in North America, one became president of a large psychiatric association for one year and another heads a large pediatric clinic in the United States.

Substance use is continued despite knowledge of having persistent and recurrent physical or psychological problems that is likely to have been caused or exacerbated by the substance.

Drug dependent patients have to continue to use the drugs very often against their own will. It is not voluntary for them. Some are willing to keep on using them because they expect that the drugs will really help them recover but when they are given the option to follow an orthomolecular program they will do so with alacrity. I have seen very few patients who really like to feel drugged.

The Tranquilizer Psychosis

This morning a young schizophrenic woman came to see me. She had been on thioridazine and doing quite well. I added the orthomolecular program and she began to improve. However the psychiatrist she had been seeing regularly started a study on olanzapine and persuaded her to switch to 15 mg daily. He made her promise that she would not stop the medication for two years. According to her father she became less psychotic but according to the patient the price was so great it was not worth it. She had gained 50 pounds. At age 19 this was a terrible blow to her self-esteem and to her future social growth. She begged her psychiatrist to switch back to thioridazine but he would not, dismissing her concern with the blunt uncaring and insensitive statement, “It is better to be fat and normal, than thin and psychotic.” She was improving on the orthomolecular program anyway but as far she was concerned she had been better off lean and good looking even if she was a bit more psychotic. It was clear to me her psychiatrist was more interested in the drug study he was doing than he was in her overall welfare. She decided, and her parents agreed, that she would drop out of the study and probably not see that psychiatrist anymore. I persuaded her to try a lower dose and wait for two weeks until she had a chance to talk it over with him.

I have not seen any studies discussing the most toxic effect of drugs, compared to which tardive dyskinesia is minor. This is that tranquilizers create a tranquilizer psychosis. It is not surprising that this is totally ignored. The first psychiatrist to point out that tardive dyskinesia was

caused by tranquilizers was almost totally ostracized for several years after his first report appeared. The drug companies certainly will not find it advantageous to refer to this major problem induced by their favorite drugs, and psychiatrists who have been nurtured on the idea that these are the only drugs will find it very difficult to change their point of view.

If you do not believe that tranquilizers cause a psychosis, start taking 15 mg of olanzapine today and stay on it for a few months and see what happens to you. Ask your family what they think of your condition, i.e. if you are still working. The tranquilizer psychosis is a mixture of the original psychosis under partial control combined with the toxic effect of these drugs. The following table shows the similarities and difference between the natural psychosis and the tranquilizer psychosis. The severity of the tranquilizer psychosis is dose related.

This diagnosis fits the DSM-IV.[2] Classification 292.11 applies to sedative, hypnotic, anxiolytic psychosis with delusions; the 292.12 classification fits sedative, hypnotic, anxiolytic psychosis with hallucinations. The Merck Manual[3] lists anti-psychotic drugs under the heading anti-anxiety drugs or anxiolytics.

Comparing schizophrenic psychosis with the tranquilizer psychosis

Symptoms/signs	Schizophrenia	Tranquilizer Psychosis
Perception	Voices	Not as severe, or gone
	Visions	Same
	Illusions	Same
Thought Disorder		
Content	Paranoid	Not as intense
	Delusional	Same or less
	Ideas of Reference	Same or less
Process	Blocking	Not as intense
	Memory	Same or worse
	Concentration	Same or worse
Mood		
	Depression	Same
	Agitation	Less
	Anxiety	Less
	Apathy	More
	Disinterest	More
Behavior		
	Hot	Cool
Physical Toxicity	None	Tardive dyskinesia
		Nausea
		Brain damage
		Weight gain
		Diabetes
		Impotence

The internet contains many reports on the damaging effect of tranquilizers on the brain. L. Stevens, a lawyer who defends many psychiatric patients, describes the many toxic side effects of these drugs. He writes, "These major tranquilizers cause misery–not tranquility. They physically, neurologically blot out most of a person's ability to think and act, even at commonly given doses. By disabling people, they can stop almost any thinking or behavior the therapist wants to stop. But this is simply disabling people, not therapy. The drug temporarily disables or permanently destroys good aspects of a person's personality as much as bad. Whether and to what extent the disability imposed by the drug can be removed by discontinuing the drug depends on how long the drug is given and at how great a dose. The so-called major tranquilizer anti-psychotic/neuroleptic drugs damage the brain more clearly, severely, and permanently than any others used in psychiatry."

Joyce G. Small, M.D., and Iver F. Small, M.D., both Professors of Psychiatry at Indiana University, criticize psychiatrists who use psychoactive medications that are known to have neurotoxic effects, and speak of the "increasing recognition of long lasting and sometimes irreversible impairments in brain function induced by neuroleptic drugs. In this instance the evidence of brain damage is not subtle, but is grossly obvious even to the casual observer!" According to Conrad M. Swartz, Ph.D., M.D., Professor of Psychiatry at Chicago Medical School, while neuroleptics relieve psychotic anxiety, their tranquilization blunts fine details of personality, including initiative, emotional reactivity, enthusiasm, sexiness, alertness, and insight.

Side effects, usually involuntary movements, can be permanent and are hence evidence of brain damage. A report in 1985 in the Mental and Physical Disability Law Reporter indicates "courts in the United States have finally begun to consider involuntary administration of the so-called major tranquilizer/anti-psychotic/neuroleptic drugs to involve First Amendment rights because...anti-psychotic drugs have the capacity to severely and even permanently affect an individual's ability to think and communicate." In Molecules of the Mind: The Brave New Science of Molecular Psychology, Professor Jon Franklin observed: "This era coincided with an increasing awareness that the neuroleptics not only did not cure schizophrenia - they actually caused damage to the brain." "In severe cases, brain damage from neuroleptic drugs is evidenced by abnormal body movements called tardive dyskinesia. However, tardive dyskinesia is only the tip of the iceberg of neuroleptic caused brain damage. Higher mental functions are more vulnerable and are impaired before the elementary functions of the brain such as motor control." Without doubt, Stevens has captured the essence of the tranquilizer psychosis.

In a recent report, Madsen et al[4] found a significant association between the amount of tranquilizers taken over years in grams and cerebral cortex atrophy. The estimated risk of atrophy increases by 6.4% for each additional 10 g of tranquilizer drug (in chlorpromazine equivalents). Gur et al[5] reported that tranquilizers increased subcortical volumes in schizophrenic patients. These changes were not present in patients not on this medication. They suggested these changes were in response to receptor blockade and could decrease the effect of treatment. In other words these drugs damage the brain and decrease the odds these patients can ever recover. Are we preparing the ground for the next major pandemic of illness with millions of chronic schizophrenic patients becoming more and more brain damaged as they are forced to remain on their tranquilizers. And when it is fully upon us, what are we going to do about it?

Meyer Gross remarked many years ago that tranquilizers convert one psychosis into another, a natural psychosis into an

iatrogenic psychosis, the tranquilizer psychosis. This is characterized by increasing brain damage as the dose in grams increases (daily dose multiplied by number of days on that dose) and by the clinical description of this psychosis given in this report. They convert hot into cool symptoms[6] which are much more tolerable and allow the patient to be cared for at home, to be discharged from hospitals too soon, and to make available the city streets for their care and shelter. The objective of therapy should be to cure the patient in the sense that one cures diabetes. It is to remove symptoms and signs, to make it possible for patient and family to get along reasonably well, to permit the patient to get on in the community, properly housed and reasonably comfortable, and to pay income tax. One of the basic principles of medicine, to do the patient no harm, must be obeyed. I estimate that fewer than 10% of all schizophrenics treated in North America ever achieve this state of well being with or without tranquilizers when this is the only treatment.

Tranquilizers do initiate the recovery process in schizophrenic patients and this produces the illusion that they will eventually lead to a recovery. However, as the recovery process continues, that person's biochemistry becomes more normal and then begins to respond to the drug as if they were normal, i.e. they become sick. Tranquilizers make normal people (including schizophrenics) sick. This was established in Russia, under the previous communist controlled regime, when dissidents were considered schizophrenic because they were dissidents and placed on Thorazine. They did become psychotic with the tranquilizer psychosis.

This then is the dilemma. How can patients benefit from the moderate improvement induced by the drugs and at the same time be prevented from becoming psychotic from the drug? The usual way is to withdraw the drug, but in most cases the original psychosis recurs and this process is repeated over and over. One can very slowly decrease the amount of drug, but in most cases the same disease recurs. There is no escape because when the drug dose is so small that the side effects are gone, its therapeutic effect is also gone.

Orthomolecular Psychiatry

Orthomolecular psychiatry provides a third pathway, a pathway toward health. Nutrients have no side effect in the recommended doses. They gradually start the process of real recovery in most cases but they do so slowly. It takes at least two months before they kick in, but once they are effective the disease seldom recurs as long as the nutrients are taken. This means that one can combine the therapeutic effect of nutrients, which is slow but enduring, with the rapid therapeutic effect of the drugs, and as the patients begin to recover the amount of drug is slowly decreased until the dose is nil or so close to it that there are no side effects. I have several patients on haldol 1 mg daily and they remain well on this dose. Xenobiotic psychiatrists provide the schizophrenic patients with two choices: remain psychotic without drugs or become psychotic with drugs. It is not surprising so many patients have to be forced by legal sanction or by parenteral administration to take drugs.

If the tranquilizer drugs are not withdrawn as the patients begin to recover on orthomolecular therapy there will be no response or no apparent response. There may have been a change to the original schizophrenic state but this will be masked by the tranquilizer psychosis. If, therefore, investigators not aware of these facts conduct double blind studies, they will maintain the same dose throughout the study and will see little change with or without the orthomolecular therapy. Nutrients do not reverse or cure tranquilizer psychosis. It is vital that the amount of drugs be reduced as recovery begins, for only then will

the investigator see the real effect of the treatment and only then will patients and their families observe the real recovery which has occurred.

Recently I saw a young schizophrenic man, age 19. He has been psychotic several years. His mother told me that she had him on the orthomolecular program with adequate doses of vitamins for six months but during that time saw no response. Then she remarked he had been taking olanzapine through that period. This means that we do not know what really happened. I started him on the correct program and instructed her to start reducing the dose very slowly in about two months, to take about a year in reducing it to a very low level or zero. I fully expect that this time she will see the usual response.

The six prospective double-blind, placebo controlled trials we conducted in Saskatchewan between 1952 and 1960 did not include drugs in our treatment protocol. Medication was allowed but this was decided by the physician in charge and appeared equally in all groups. As usual the medication was decreased as patients began to recover. The results are described in my book, Vitamin B_3 and Schizophrenia: Discovery, Recovery, Controversy, (Quarry Press, Kingston, ON 1999). We were fortunate these drugs were not the major treatment modality since it now appears very likely that had the drugs not been decreased in dose there would have been much less difference between placebo and active treatment. The tranquilizers would have washed out some of the difference and would have prevented some of the good recoveries we saw. In those early years of tranquilizer use their pernicious role in preventing full recovery was not understood. A study at the Massachusetts Mental Health center compared two cohorts of patients treated between 1945 and 1949 before tranquilizers were introduced, against a cohort between 1955 and 1959 after these drugs were in use. The earlier cohort was better off since more of them were employed and fewer were dependent on welfare.

Orthomolecular therapy is a program which combines the best of nutritional modification with large doses of a few nutrients with the best of modern drug therapy. The drugs are rapidly effective in initiating the recovery process, and the nutrient program is slow but steady and enduring. As treatment proceeds and the patients show clear evidence of recovering the drugs are slowly withdrawn. With this combination, the psychosis remains under control and the tranquilizer psychosis is not allowed to develop. If the drugs are not withdrawn the tranquilizer psychosis will develop and this will not be prevented or ameliorated by the nutritional therapy. Vitamin B_3 does not cure the tranquilizer psychosis.

Many years ago I hoped that one day we would have a drug specific against schizophrenia that would treat as well as insulin injections against diabetes mellitus. More recently I concluded that there will never be any synthetic drug that will cure these patients, reasoning that since the problem is some metabolic fault how can any compound which fits nowhere in the scheme of biochemical reactions in the body and which can only interfere ever be found to be curative. Natural molecules fit into receptors like a lock into a key and then stimulate the appropriate reaction. No other compounds will replace them. There will never be a substance that will replace any of the vitamins for example. If there is a fault which inhibits the natural interaction between molecule and its receptor it will be replaced only by compounds which fit into the receptor, i.e. by the original natural molecule. If a compound is found it will have to be so close to a natural or orthomolecular compound that it suppresses only the set of reactions which cause schizophrenia, or restores the set of reactions that allows all the other reactions

to become normal. It will have to be a minor variation of a natural compound, which can be transformed into a natural compound in the body. It will be an orthomolecular compound.

When one looks at the enormously intricate pattern of reactions involving amino acids, and essential fatty acids and all their precursors and derivatives, it is unlikely that in our lifetime such compounds will be formed. We will see a succession of evermore powerful (low dose) drugs, which will suppress some of the symptoms, and as usual the price will be that patients will not recover. There will always be an enormous price to pay and the patients and their families, not by the psychiatrists who prescribe them or the drug companies who provide them, will pay it.

–Abram Hoffer, M.D., Ph.D.

References

1. O'Donnell C, Donohue G, Sharkey L et al: Compliance therapy: a randomized controlled trial in schizophrenia. *BMJ,* 2003; 327:834-841.
2. *DSM-IV, American Psychiatric Association Diagnostic Manual,* Washington D.C. 1994
3. Merck Manual, 16th Edition, Merck Research Laboratories, Merck and Co. Inc. Rahway, N.J. 1995.
4. Madsen A, Keiding N, Karle A, Esbjerg S, Hemmingsen R: Neuroleptics in Progresive Structural Abnormalities in Psychiatric Illness. *The Lancet,* 1998; 352: 784.
5. Gur RE, Maany V, Mozley PD, Swanson C, BilkerW, Gur RC: Subcortical MRI volumes in neuroleptic-naive and treated patients with schizophrenia. *Am J Psych,* 1998; 155; 1711-1717.
6. Cool symptoms do not arouse the same degree of attention even though they are just as disabling. They include hallucinations the patient does not divulge to anyone, to thought disorder that is hidden, to moderate depression, apathy or disinterest. I define hot behavior as those which direct the attention of relatives and friends to the changes in the patient. These are extreme changes in personality and behaviour. Thus if a patient responds to paranoid delusions, is severely agitated, depressed or suicidal, or behaves in a bizarre manner, these are Hot symptoms. They quickly sort out the patients from normal peers. Many years ago a chronic schizophrenic man was admitted to the psychiatric hospital as an emergency. For a long time he sat quietly in the kitchen in his home not talking to anyone and not interacting. This behaviour was tolerable i.e. cool. But suddenly he began hopping on one foot and would not stop. Within a few days he was in hospital. These hot symptoms were intolerable and drove him into treatment.