Further Report on a Schizophrenic Patient Who Had Hyperasparaginemia

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Abstract

Perry et al (1983), discussed a schizophrenic patient with high levels of serum asparagine. A detailed clinical description of their patient is given which shows a one-to-one relationship between clinical response and an Orthomolecular treatment program. Only when optimum doses of Vitamin B-3 and Vitamin C were used did the patient show clinical improvement. On thioridazine alone the patient slowly deteriorated.

Perry, Wright, and Hansen (1983), described a patient who was found to have elevated fasting plasma asparagine levels. They considered the possibility these high levels were related to the schizophrenic metabolic abnormalities. In the clinical description Perry et al reported that "Between the ages of 24 and 39 years, the patient remained out of hospital, and his psychotic disorder ameliorated sufficiently for him to live alone and to support himself partially doing odd jobs. It is unclear whether his mental illness remitted spontaneously or whether it was controlled by thioridazine which he took continuously during this 15-year period.

I think that information published should be accurate — any other policy leads to confusion and erroneous conclusions. This paper raised three questions:

(1) Was the psychosis related to elevated asparagine levels or were these findings coincidental?
(2) Was the 15-year period during which the patient's psychosis "ameliorated" due to a spontaneous remission?
(3) Or was it due to the thioridazine?

In 1967 this patient's family first contacted me in order to obtain information about a nutritional/vitamin approach for treating schizophrenia. In January 1985 he was referred to me and I saw him for the first time. Since then he has remained under my care. I can therefore provide information which will shed light on these three basic questions.

The patient was born in June 1942. Between 1962-64 he rejected his previous diet and began to consume excessive quantities of sugar, other junk foods and alcohol. His behaviour became erratic, he became anxious and fearful, began to stutter and developed insomnia.

He was admitted to a mental hospital and remained on their in-patient list for three years but was able to live at home for lengthy periods. He was given a variety of tranquilizers and a series of ECT. Beginning in 1967 whenever he was home his parents started him on niacin 1 gram t.i.d. and ascorbic acid 1 gram t.i.d. Whenever he was admitted to hospital the physician in charge promptly discontinued this. The diet was the usual hospital diet. He had become very inactive with excessive weight gain. He appeared drugged, was sluggish, apathetic and had a poor memory.

Between 1966 and 1977 he lived with his parents and continued to take niacin and Vitamin C as before plus thioridazine 200 mg each day. His diet was sugar and alcohol free. During this decade he relapsed briefly on one occasion. Generally he was rational, able to study at a college where he achieved second year levels in geography, German and Spanish. He was socially active, held gardening and other casual labouring jobs, played rugby and soccer, swam and walked. His musical skills returned to a large degree.

Between 1977-82 he was in his own apartment with regular visits and assistance from his family. He took his thioridazine regularly, his vitamins sporadically and reverted to his previous junk diet (restaurant food, high in sugar and alcohol). He became unstable and was no longer able to hold any jobs. There was a one-to-one relationship between the quality of his diet and his behaviour. On the junk diet he developed nausea and vomiting, became

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sleepless, restless, fearful, irritable with episodes of anger, and hyperactive. Often after a binge on sugar his face would become grossly swollen, affecting mouth and throat. He breathed with difficulty and would become loud and hysterical. On one occasion he was admitted to a psychiatric ward for two days and was diagnosed as having an allergy-induced psychotic reaction. He continued to deteriorate until an accident in April 1981 when he broke his right humerus. For two years he had not taken any medication or vitamins. Following the accident he was taken off all medication while in hospital for ten days to promote healing and was given antibiotics.

In September 1981 he was tested by Dr. Perry with results described in his report to *Biological Psychiatry*.

He was admitted to hospital November 17-29, 1981, for further examination. His attending physician described him "as a polite cooperative man in no apparent distress. He did show some evidence of thought disorder, but he was not psychotic." In hospital thioridazine was again discontinued and he was started on propranolol 320 mg t.i.d. for hypertension even though the physician recorded "the propranolol made no significant difference in his blood pressure".

On discharge he was agitated, continually paced the floor, had a poor appetite, vomited, suffered from diarrhea, was weak and anxious and experienced hallucinations.

He was readmitted December 9-22, 1981. The physician in charge concluded the propranolol had not helped his schizophrenic psychosis. He was discharged on a lower dose plus fluphenazine 2 mg per day. After this discharge he was heavily drugged, agitated, restless, smiled inappropriately, shouted out of his apartment windows at night and disturbed his neighbours with loud music and his yelling. This was new psychotic behaviour never previously exhibited.

He was readmitted January 8-19, 1982, because of this abnormal behaviour and continued to behave this way in hospital. He left hospital on his own. He was to take fluphenazine 15 mg per day. He remained confused, completely out of contact with reality, hallucinated, with all the previous symptoms present in exaggerated form. During March 1982 he lived alone. He was charged with indecent assault and was admitted briefly to another hospital psychiatric ward. Since then he has lived in the following institutions:

1. Psychiatric ward, April 1982.
2. Group home, May 1982.
3. The same psychiatric ward, June 1982. Emergency department after falling several times, was very drugged.
4. Same hospital, July 1982.
5. A boarding home, August 1982.
6. Same hospital, August 13 to December 17, 1982.
7. Another mental hospital, December 18, 1982, to June 1983.
8. A boarding home, June - August 1983.

Throughout these various admissions me dication was continually readjusted and thioridizine re-started.

9. Another boarding home, August 1983 -June 1984.
10. Same hospital, June 1984.
11. Same hospital, June 23, 1984.
12. Same hospital July 14, 1984. Further admissions (13-18): July 21, July 25, July 31, August 5, August 16 and August 24, 1984. From July 1984 there was a gradual improvement. He was more rational but still hallucinated (voices).

I saw him for the first time January 14,1985. He was brought to me by his parents. They had decided they could help him more if he were once more placed upon an Orthomolecular treatment program. When I examined him he continually heard voices, had visual hallucinations and was convinced everyone was watching him. The voices emanated from a guru, or from police, or from nurses who wanted him back in hospital. He believed people were laughing at him. He was very depressed, lonely, nervous and tired. At this time he was taking thioridazine 200 mg q.i.d., chlorpromazine 400 mg per day and methyl dopa for hypertension. He was still living in the same group home. This home had agreed to follow my recommendations. He was obese having gained 50 pounds over the previous three years. He was started on the following nutrients: niacin 1 gram t.i.d., ascorbic acid 1/2 gram t.i.d., calcium 500 mg b.i.d., magnesium oxide 420 mg o.d. and cod liver oil 1 tablespoon per day to be added to a sugar-free diet. The calcium and magnesium were used to try and bring down his high blood pressure. He was then to be monitored by his family physician. I discontinued the chlorpromazine.

I saw him again March 20, 1986. There was

a striking improvement both physically and mentally. He had lost 25 pounds and no longer appeared obese. He needed to lose another 15 pounds. The thioridazine had been decreased to 400 mg per day. His mother had increased his Pyridoxine to 500 mg per day and added zinc gluconate 50 mg per day, and placed him on a gluten-free, milk-free program. It was now possible to talk to the patient. He still heard voices but was no longer as troubled by them, nor did he act upon them. He was able to avoid talking about his delusions so that people around him were relatively unaware of them. His parents were delighted with the improvement. He was now almost what he had been like when he had last been on a proper nutrition vitamin approach many years before. His mood was normal.

Briefly, this patient's history can be divided into a series of phases related to the treatment given him.

Relation of Degree of Psychosis to Treatment

Dates	Treatment	Response
1962 - 1966	Junk food, ECT, drugs. 3 years in hospital.	None
1966-1977 1977-1981	At home. Proper diet, vitamins, thioridazine 200 mg.	Much improved
Sept./81 -Jan. 19/82	Own apartment and institutions. Junk food. Sporadic use of vitamins. More steady use of thioridazine.	Deteriorating Eventual fracture
	Junk diet, no vitamins, variety of drugs, 3 admissions. Not on thioridazine.	Marked deterioration to point was worse than ever before.
1982 - 1984	Another 15 admissions to hospital. No vitamins, thioridazine.	Remained psychotic but was better by end of 1984.
Jan. / 85 to present	Boarding home, on vitamins, proper diet and thioridazine 800 mg decreased to 400 mg, chlorpromazine 400 mg discontinued Jan. 15/85.	Has improved steadily and has regained state while on previous full program end of 1977.

Discussion

It is impossible to conclude that asparagine levels and a disturbance in asparagine metabolism was relevant in this psychosis. It might be. Perry et al tried to correct this by using Pyridoxine 1000 mg per day for a few days and saw no response. Yet this patient's parents found an additional burst of improvement when they increased Pyridoxine from 250 mg to 500 mg per day. But it was made part of the program combined with both zinc and magnesium which are essential for Pyridoxine to be most therapeutic. It would be interesting to repeat the earlier biochemical studies, but it is doubtful his parents would allow him back into the psychiatric unit again where the tests had originally been done.

The second hypotheses was the suggestion by Perry et al that the 15-year improvement was a natural remission. This is a curious idea which goes counter to all the clinical facts in this patient's case. The facts are simple. Whenever this patient is on a good diet supplemented by vitamins B-3 and C with one tranquilizer, thioridazine, he improves until he can function well in the community. He had reached a level where he was able to study and hold several jobs. When he stopped his vitamins, broke his

diet, and kept on with thioridazine he relapsed and deteriorated until he was more psychotic than ever and required at least 18 admissions over a three-year period. When the original therapeutic program was resumed he once more began to improve and his prognosis is very much better. He may be able to do without thioridazine in a couple of years or may require 100 mg per day or less. Perry et al were apparently not aware of this patient's history, which is surprising because his parents were extremely anxious for the vitamin program to be continued. It was no secret. Before anyone can accept a natural remission hypothesis they will have to explain why there is this strong relationship to the presence or absence of proper nutrition and vitamin supplements.

Could his natural remission have been due to thioridazine alone? This is unlikely. It is clear this is the tranquilizer which has been most helpful to him and which did not make him worse. But when he went off his nutritional vitamin therapy thioridazine alone did not prevent him from gradually relapsing and deteriorating.

There is only one logical conclusion as the clinical data speaks for itself. I do not think one should dignify the placebo hypothesis by discussing it, nor to ascribe this improvement to my personality as I have only seen this patient on two occasions. During his first visit he was too psychotic to even be aware of the interaction. The conclusion is that this one patient does reasonably well only when he eats properly, takes vitamins B-3 and C and small quantities of thioridazine.

One might further conclude that he represents only one class of responders of which he is the sole member. I prefer to conclude he represents a large class of schizophrenic patients who will respond much better to Orthomolecular treatment than to tranquilizers alone.

Reference

Perry, TL, Wright, JM and Hansen, S: Hyperaspar-aginemia in a schizophrenic patient. Biological Psychiatry, 18:89-97, 1983.