Editorial

Schizophrenia: Its Biochemistry, Psychology and Treatment

For the past 55 years I have been studying, investigating, living with and treating schizophrenic patients. No, my wife, Rose, and my three children were not schizophrenic nor was I until I took adrenolutin, and then it lasted only two weeks.

With my wife's cooperation we took a young woman, who had been a resident in the mental hospital at Weyburn, Saskatchewan for 14 years, into our home in Regina in 1953. She is described in our book *How To Live With Schizophrenia*[1]. I believed that I would be in a much better position to research this dreadful disease if I knew a lot more about it. An admissions IQ test put her into the range around 25, that is in the idiot range. Of course this was totally wrong, as no IQ test is valid when administered to very ill patients. During her stay in the hospital she was one of their most difficult, sickest patients.

The hospital, in common with all mental hospitals and all psychiatry in 1950, did not know how to treat schizophrenia but psychiatry at that time was not overly impressed with either drugs as none were known nor with psychoanalysis as Freud's work was unknown. Therefore the doctors on staff were prepared to try anything that promised to help. Mary (not her real name) was given camphor injections to cause convulsions. This was the forerunner to Electroconvulsive therapy (ECT), which she also had. Eventually whenever she became violent and aggressive she would be given another series of ECT perhaps yearly or more often. Luckily for Mary there was no one on staff who knew how to do lobotomies or she might have had one.

One of her favorites activities was to smash all the windows in sight. Perhaps this was a way of trying to escape. At the same time she learned how to be a very good cleaner and she was very fond of babies and children. With Dr. H Osmond's approval we took her into our home in Regina. I did learn a lot, as did Rose, perhaps more than she had expected to. The first few months were very difficult but after I knew Mary well I started her on niacin 1 gram after each of three meals. She began to get better, lost her auditory hallucinations, recovered, and, in 1955 when we moved to University Hospital, now Royal University Hospital, in Saskatoon, we took her with us. She got a job on the cleaning staff of the hospital, got her own apartment and became one of their best workers. She was one of the cleaning staff wearing a colorful, cheerful uniform when Princess Margaret toured the hospital before it was renamed. Mary exclaimed "My how beautiful you are". Royalty and my patient were very friendly to each other. Mary died about five years ago from heart failure.

I learned from Mary how to live with and how to understand this disease. She was a very fine person, loved our three children, loved animals and had several pets. We remained friends. She often came to our house to help Rose. They had a very good relationship. Between 1954 and her retirement she paid income tax, completed her own taxation forms and only on occasion would come to me for help or to protect her against uncaring individuals with whom she had to exist. Orthomolecular treatment (shelter, good nutrition, civility and the correct nutrients) saved Mary from a lifetime of chronic schizophrenia and probably early death and saved the government of Saskatchewan nearly one million dollars in costs, had she remained in hospital. She was never treated with drugs.

I wanted to learn even more. Dr. Osmond had brought with him his skills and enthusiasm about using the hallucinogens as a way to understand the disease. We read dozens of books written by recovered

patients who described what it had been like. I took LSD twice in my home, carefully supervised by Dr. Osmond and others and we both also took adrenochrome and adrenolutin, the oxidized derivatives from adrenalin. After taking adrenolutin I was paranoid and depressed for two weeks. I now understood what it is like. It is not very pleasant.

This was at the beginning of our research, which has been reported in many papers in the psychiatric and medical literature[2-4] and in my books.[5] This led to our biochemical studies with adrenochrome, with adrenolutin, with the mauve factor later identified as kryptopyrolle, with the use of large doses of vitamin B_3 as a treatment. After thinking about, investigating, living with and treating over 5,000 schizophrenic patients since 1950, I will distil the information I have gained and present it as a working hypothesis of schizophrenia. I will provide a few references to the most important sources. This will be a broad overview of the syndrome as I see it. I am sure it will not be the popular view but it is mine and I am prepared to fight for it. As Dr. Joseph Goldberger said to his wife one day when she complained about the lack of appreciation of his work "I know what I have done, and it is a satisfaction to my soul which no one on earth can take from me." It led to Orthomolecular therapy and a way for these unfortunate patients to recover, to become useful members of and to contribute to society, and to pay income tax.

The Schizophrenic Syndrome

A syndrome is a coexistence of a number of symptoms and signs which usually points to an organ system or hormonal disease but which may be caused by different factors. The causes are different but the clinical description, the end state, is the same. A good example is the pneumonia syndrome. If you are having pain in your chest, worse on breathing, you have fever and have difficulty breathing, you have pneumonia. But it may be due to an infection from bacteria, from yeast, from viruses, from toxic elements such as silica or may be due to cancer. Before X rays were discovered it was very difficult to determine the cause; of course it did not matter since there was no treatment. I had pneumonia when I was around 10 years old. I could not understand why my mother was so worried nor did I know that in those days it had a high mortality rate. I was treated with mustard plaster and was well in three days but I am certain not from the mustard plaster. Today the reasons for the pneumonia will be determined before treatment can be started. The syndrome points toward the system or organ but it does not indicate the treatment that should be used. In the same way schizophrenia is a syndrome and is precipitated by a large number of different trigger factors.[6] Treatment will not be optimal until the reasons for syndrome are known, even though the syndrome is similar for all the trigger factors. Unfortunately too many physicians still use a mustard plaster approach in treating their schizophrenic patients.

Syndromes were recognized a hundred years ago. The differential diagnosis one had to think about in 1900 was dementia praecox, scurvy, pellagra and chronic syphilis of the brain. They all caused the schizophrenic syndrome. In 1900 there was no treatment so that it did not matter. Since then scurvy and pellagra have been conquered, syphilis of the brain is readily treated with antibiotics and dementia praecox, still with us, has been renamed schizophrenia. The other three forms of psychosis caused by those three known factors have been torn from the psychiatric fold and became the province of internists and general practitioners.

Dr. John Conolly[7] described insanity very simply. It was a disease of perception combined with an inability to tell whether

these changes were real or not. I consider this a marvellous operational definition which has not been bettered since that time and which has been confirmed by the studies of Lewis and Pietrowsky. When he wrote this definition, about 1840, it did not appear that he considered it new or original. Dr. Willis (of Circle of Willis fame) had the same view about insanity much earlier. We cannot be totally certain which psychosis they were discussing but it was called insanity and must have been largely what we today call schizophrenia.

Briefly, it means that the syndrome is characterized by having perceptual changes, most known commonly as auditory and visual hallucinations, voices and visions, to which the patients respond as if they were true. These changes apply to all of the senses and there is an enormous variety of changes. The inability to determine that these changes in perception are not real is called thought disorder and again there is no limit to the variety of delusions that patients will suffer. Conolly described the case of a depressed woman who believed her husband was dead because she could see his ghost perched in the tree outside the window of her hospital room. She had a vision (perceptual change) which she assumed was true (thought disorder) and she responded with depression. When her husband was told, he went into her room; before he had been advised not to. Upon seeing him she fainted, arose and said let's go home. The visual hallucination must still have been there but she also saw the real person, lost her delusion and of course no longer needed to respond with depression.

Another example was one of my patients who heard God telling her to burn her neighbor's house down; believing that it was God speaking, she did. She had a perceptual disturbance and thought disorder and she was schizophrenic. She recovered on orthomolecular treatment and has been well many years and running her own company. In *How To Live With Schizophrenia.* (now *Healing Schizophrenia*) we describe our views about this method of understanding what is going on in the mind of many of these patients.

Professor Nolan Lewis and his associate at Columbia University re-examined the diagnosis of a large number of patients who had been admitted many years before and had been diagnosed as manic-depressive. At the time of re-examination, half of them had been re-diagnosed schizophrenic. They examined the admission charts very carefully to answer the question - "Had the condition changed from manic-depressive to schizophenic or had the original diagnosis of schizophrenia been missed?" When they re-examined the charts they found that if the admitting doctors had taken into account the presence of these perceptual changes they would have accurately diagnosed them as schizophrenic and there would have been no change in diagnosis from manic depressive to schizophrenic. Dr. Osmond and I adopted the Conolly classification and based our HOD test upon it. This is a very accurate diagnostic test using cards to be sorted into true or false categories.

Conolly emphasized that perceptual change as primary. When Bleuler wrote his book, *The Schizophrenias,* perceptual changes were given a secondary role and thought disorder became the main diagnostic factor. Bleuler's description became the norm. This is a pity since it is a lot more difficult to use and to obtain any uniformity in diagnosing. Modern psychiatry corrupted both of these classifications but in general tends not to diagnose schizophrenia unless hallucinations and delusions are present. It has hedged its bet by assigning waiting times before the condition can be diagnosed. In essence it matters little since both bipolar and schizophrenia are treated in the same

way with the same results. I consider that schizophrenia is a perceptual disease, that there is an error in the sensory system so that the brain misinterprets stimuli in an abnormal way. The closest to the actual experience may be induced by the hallucinogens, to which so many modern young and middle aged men and women have exposed themselves, giving a temporary schizophrenic experience, which can be good (psychedelic) or bad (psychotomimetic).

Schizophrenia is characterized by changes due to sensory misinterpretations of afferent stimuli and inability to judge that these changes are not true.

Need to Understand Schizophrenic Behavior

Connolly's explanation of schizophrenic behaviour has not been accepted by psychiatry. In essence, he believed that if a person suffered from abnormal perceptual symptoms and responded to these as if they were true, this would result in bizarre behaviour. He gave several illustrations including the depressed woman who saw her husbands ghost outside her window perched in the tree. I have seen many examples. A very common delusion used to be that of being poisoned. This was caused by a change in the sense of taste, and food tasted flat, or bitter. If the person realized that the change arose from some abnormality in his sense of taste he would deal with this normally. Very often a zinc deficiency will do this. But if he concluded that the change in the sense of taste is due to someone tampering with his food, he is then psychotic and the reaction may be devastating. I have had patients who believed their wives were doing so and who refused to eat any food unless they cooked it themselves. There is no point arguing with them as their choice is between what their sense of taste tells them and denying the validity of their sense of taste. Sometimes it helps by telling them of the possibility their sense of taste has changed and that something will be done about that.

These paranoid delusions have become very rare. I think this is due to the fact that many years ago most medicines tasted bitter or awful and therefore it was easy to associate bad taste with poison being added. For the past decade drug companies have made their products sweet and much more palatable; this has removed the paranoid delusion of being poisoned. Another patient while walking west down town in the late afternoon suddenly saw a vast illumination of the sky, heard a loud voice boom at him which said "You have syphilis and you must have intercourse with a virgin if you are to be cured". He concluded God had spoken. He immediately began to chase after a young girl who had been walking in front of him and he soon found himself in our psychiatric ward. When I asked him why he had behaved in this way, he told me the whole story. In these examples the perceptual changes combined with the belief that they were real caused the psychotic behaviour. When a person commits a clearly bizarre act the usual reaction of the public is to complain and wonder why would he do this. But I have not seen anything come out later during the investigation which indicates that any attempt was made to get inside their brain, inside their experience and determine why they behaved as they did.

A horrible example was the case of a young schizophrenic patient discharged from a mental hospital who early one morning in a senseless rampage killed every member of the Hoffman family except the baby crawling on the floor.[8] He told me that he could no longer resist the orders he was given by the devil whom he saw as six and half feet tall with the head of a pig and who threatened him with loss of his soul.

Psychotic behaviour is comprehensible if one determines the perceptual distortions.

What Causes Perceptual Changes

Any change in the operation of the biochemical reactions in the synapses in the brain in the area of the brain which interprets these changes will cause these misinterpretations. The best examples are the experiences induced by the hallucinogens like mescaline and LSD. These compounds interfere with the transfer of information from cell to cell. This was first clearly pointed out by Osmond and Smythies in 1952, when they proposed that there were substances in the schizophrenic patients with the properties of mescaline and related to adrenalin. An examination of the known hallucinogens quickly showed that the indole nucleus was common. Discolored adrenalin had slight hallucinogenic properties and the pink substance was the oxidized derivative of adrenalin, called adrenochrome. This became our adrenochrome hypothesis of schizophrenia.

When we first wrote abut the adrenochrome hypothesis[9] we were not aware of the other chrome indoles that the body oxidizes from the other catecholamines. To keep this discussion simpler, I will write only about adrenochrome but this does not exclude dopachrome or other unknown derivatives from major roles. Adrenochrome is made in the body from adrenalin and similar substances, such as dopamine and noradrenalin, have their characteristic oxidized derivatives; dopachrome from dopamine, noradrenochrome from noradrenalin and adrenolutin, which comes from adrenochrome, are hallucinogens. Adrenochrome, like LSD, interferes with synaptic function in the brain. There is some evidence that LSD increases the formation of adrenochrome, as does cocaine.

Adrenochrome and similar compounds in common with the hallucinogens cause these perceptual changes. Trigger factors promote the excessive oxidation of adrenalin to adrenochrome.

Factors which Trigger Excessive Oxidation of Adrenalin to Adrenochrome

Any trigger factor which increases oxidation will cause and aggravate already existent schizophrenia. Excessive oxidation promotes the formation of adrenochrome. This will result from excessive release of adrenalin, from an increase in enzymatic oxidative and autocatalytic activity and from a deficiency of antioxidants, which the body uses to control excessive oxidation. Triggers which increase oxidative stress are severe stress, the release of adrenalin and noradrenaline, and too much copper and iron.[10] Infections whether bacterial, viral, or fungal may also be trigger factors. Fever will also increase oxidation. Hypothyroidism is also a trigger factor

On the other hand, antioxidants will be therapeutic. The antioxidants are vitamin B_3 as part of the NAD<–>NADH system, vitamin E, the main fat soluble antioxidant and vitamin C, the main water soluble antioxidant and antioxidants made in the body like glutathione, N-acetyl cysteine, and selenium.

Nicotinamide Adenine Dinucleotide Deficiency

The adrenochrome hypothesis was developed in order to help us in our search for effective treatment for schizophrenia. If adrenochrome were a main factor it follows that anything that decreases the formation of s adrenochrome will be therapeutic. At the first meeting in 1952 of the Saskatchewan Committee on Schizophrenia Research our attention was drawn to niacin as a potential treatment. The biochemistry suggested that giving patients large amounts of this vitamin would decrease the production of adrenalin from noradrenalin and make less avail-

able to oxidize to adrenochrome. This has still not been examined and whether it decreases adrenalin production I do not know. But it is not an objective of a hypothesis to be correct. The objective is to direct research into fruitful areas and this it has done. Even if it turns out that the adrenochrome hypothesis is dead wrong it will not negate the fact that niacin is a very valuable treatment for this devastating disease.

It was not entirely a leap from the biochemistry to the clinic. It was already known that pellagra, a niacin deficiency disease, was a major cause of schizophrenia until the raging pandemics of this disease of poverty in the South East United States were brought under control by the addition of niacinamide to flour. In some years 300,000 pellagrins were diagnosed. In some years up to one third of the admissions to mental hospitals were pellagrins who were also psychotic.

Pellagra is characterized by four Ds; dermatitis, diarrhea, dementia and death. Almost all patients have terrible skin lesions, which gave it its characteristic name, *pelle agra*, Italian for dark skin. But many pellagrins did not have skin lesions. It was associated with exposure to the sun which made these areas much more sensitive. Diarrhea was very common and very serious. The dementia was a schizophrenic syndrome. It was clinically not distinguishable from schizophrenia unless one took a history of poverty and pellagra- inducing diets. When pure niacin became available it was used as the diagnostic test. If psychotic patients in mental hospital were given niacin and responded within a few weeks they were called pellagra. They used doses below 500 milligrams daily. If they did not respond they remained schizophrenic. I can understand the illogic of this behaviour because both pellagra and schizophrenia were so complicated and so little was known about them. Had the pellagrologists in the 1930s not been preoccupied with denying that pellagra had anything to do with schizophrenia they might have asked themselves, "If these conditions are so similar that we cannot tell them apart, maybe they are really the same and that difference is a matter of how long they have been sick". They had already observed that chronic patients did not get well in a few weeks and that they needed at least 500 milligrams of niacin to remain free of their symptoms. That dose, in 1935, was enormous. Black tongue in dogs was the equivalent and dogs kept sick too long did not recover with the usual vitamin dosages. They too needed very large doses. It is clear that the longer one suffers from a deficiency of B_3 the more will be needed thereafter to make up for the defects induced by the prolonged deficiency. We knew that niacin prevented and cured pellagra and its psychosis, we knew that it was safe with an LD 50 of about 4.5 grams per kilogram or for a 70 kilogram patient would mean several hundred grams daily. But this figure is meaningless since no one has actually determined how much niacin it would take to kill people; there are no deaths from niacin excess, only hundreds of thousands of deaths from a niacin deficiency called pellagra.

Pellagra is caused by a diet too low in protein, too low in the amino acid tryptophan, too low in vitamin B_3, too low in isoleucine as well as being too rich in leucine and too rich in foods like corn which binds niacin and prevents its absorption by the body. Tanner working with Goldberger[11] reported that patients given tryptophan were also cured of pellagra because enough was converted into niacin and that skin lesions typical of pellagra healed more rapidly. I suggest that pellagra is a double deficiency disease lacking at least two factors, tryptophan and niacin. Tryptophan alone cannot be used to treat schizophrenia because so little is converted into niacin. But manic-

depressive patients have been given 12 grams daily and it has been valuable in stabilizing their mood.

Pellagra is caused by a multiple deficiency of many nutrients due to the consumption of the wrong food, and is an offshoot of poverty and ignorance. Therefore treatment of pellagra must follow the nutrition rules discovered and popularized by Goldberger 90 years ago. If these patients have the normal capability of converting tryptophan into NAD they will not need vitamin B_3 supplements in large doses for treatment. The usual average intake that is adequate for most people should be adequate for them as well. Adding B_3 will of course accelerate recovery and it is very important that every one be given enough to take into account the needs of those of us who are not able to make enough NAD from the tryptophan in our diet. Schizophrenic patients are different. They are psychotic because their biochemical systems are not able to protect them against the oxidative stress and lack of anti oxidants. Giving them more tryptophan will not be sufficient. They will need very large doses as we discovered in 1952. They are like the chronic pellagrins who have been sick too long and therefore need very much more to be free of symptoms or like the dogs with black tongue who have been kept in that state too long and will also need much more vitamin B_3. The ideal treatment for schizophrenia therefore must include all the elements of a good diet with adequate protein intake and optimum doses of vitamin B_3 whereas for pellagra the extra large doses of vitamin B_3 are not needed unless they have been sick too long.

The condition of patients who are very close to having pellagra is described by Tom Spies et al[12] who wrote, in 1938, in his paper, "The Mental Symptoms of Pellagra":"Sub-clinical pellagrins are noted for the multiplicity of their complaints, among which are many that are usually classed as neurasthenic. The most common of these symptoms are fatigue, insomnia, anorexia, vertigo, burning sensation in various parts of the body, numbness, palpitations, nervousness, a feeling of unrest and anxiety, headache, forgetfulness, apprehension, and distractibility. The conduct of a pellagrins may be normal but he feels incapable of mental or physical effort, even though he maybe ambulatory." I provided a detailed description of pellagra, its physiology and biochemistry in the classical book edited by Hawkins and Pauling, *Orthomolecular Psychiatry. Treatment of Schizophrenia*.

Today, children with subclinical pellagra[13] as it was described over 50 years ago, would be classed as either hyperactive, or as having one of the Attention Deficit Disorders given to such children in the American Psychiatric Association Diagnostic Manual DSM IV.

Sources of Niacin

In 1973 I wrote a very detailed and comprehensive account of the biochemistry of pellagra and of schizophrenia and their relationship to the pyridine nucleotide cycle, to tryptophan and to vitamin B_3[14]. I suggested "It is possible and, if the views presented here are reasonably close to the truth, even highly probable, that the genetic errors which underlies the schizophrenias is an enzymatic block between tryptophan and NAD. The postulated block between tryptophan and NAD may provide an evolutionary advantage in the presence of adequate exogenous vitamin B_3". Hoffer and Foster discuss this in detail.[15]

Niacin is not a true vitamin in the strictest sense of the term since it can be produced in the body from the amino acid tryptophan. Nevertheless, the synthesis of niacin from tryptophan is a very inefficient process and 60 milligrams of the amino acid are necessary to provide

1 milligram of niacin. This process also involves vitamins B_1, B_2 and B_6.

Hoffer and Foster write "It is clear, therefore, that humans have the ability to synthesize niacin, but this process is ineffective and is probably in evolutionary decline. Of course, vitamin B_3 is also available from many foods. If diet contained enough of this vitamin to supply bodily requirements then there would be no need to convert tryptophan to niacin. This would liberate energy for other uses and free up tryptophan for the production of serotonin, a major neurotransmitter. It is argued here that humanity has been depending more and more on vitamin B_3 derived from diet. However, recently, niacin has become less available from food, and as a result, subclinical pellagra and other niacin deficiency disorders are becoming very widespread."

Vitamin B_3 and Treatment of Schizophrenia.[16, 17]

Our pilot studies in early 1952 were all positive. We found that we could safely give either niacin or niacinamide in large doses and that both these forms of the vitamin were therapeutic for schizophrenic patients. Amazingly all of the eight patients treated at the Saskatchewan Hospital, Weyburn, by Dr, Osmond and at the Munroe Wing by me recovered or were very much improved.

Our major two prospective double blind, randomized, placebo controlled trials were both positive. Compared to placebos we doubled the two years recovery rate by using either one of these two vitamins in doses of 1 gram three times daily after meals. Since then these conclusions have been confirmed by an NIMH sponsored and financed study, by over 50 open clinical studies, and by my experience on at last 5,000 patients treated since 1955. Some of these patients have been under my care up to 25 years. Early patients respond the quickest and chronic patients need much more time. Perhaps my chronic patients needed extra thyroid. The clinical evidence has been reinforced in a large number of medical reports and books.

I have examined possible reasons why patients deprived of the vitamin B_3 have become chronically impaired and need much higher doses for longer periods of time. This was first demonstrated by the pellagrologists in their clinical studies and also with dogs made pellagrous (black tongue). Dogs made sick by diet for a brief period of time recovered very quickly when given the vitamin but if left sick longer than six months, they needed much large doses. I also examined Canadian prisoners of war in the Hong Kong camps during the late war[18]. They were kept in horrible camps under the most severe conditions including major deficiency of calories, and all the vitamins and suffered from infectious disease and severe brutality. Nearly 25% of the Canadian soldiers died in these camps. The soldiers returned were near death and they never recovered their original health. They remained a very sick part of our Canadian population, dying from heart disease, from neurological changes, from blindness, from anxiety. The only ones who recovered did so after starting on niacin at least 3 grams daily. Soldiers in these camps aged at four times the usual rate; after 44 months in camp they had aged at least 15 years. I concluded that severe stress was of the type caused a chronic niacin dependency. I think this is now happening in many parts of the world where the combination of malnutrition, severe stress and brutality will produce a large number of very sick people.

Niacin also is therapeutic against the LSD reaction in volunteers. Since vitamin B_3 is therapeutic for schizophrenia it must decrease the oxidation of adrenalin to adrenochrome. There is some evidence for this. In Norway, Walaas and Walaas[19] found that adrenalin in the synapses lost one electron to become what he called

oxidized adrenalin. In the presence of an adequate amount of NAD the oxidized adrenalin regained that electron and reverted back to adrenalin. But if another electron was lost forming adrenochrome, this reaction was not reversible. A deficiency of the NAD^+–>NADH system would allow the continued formation of excess adrenochrome at the synapses.

Vitamin B_3 is required to prevent excessive oxidation of adrenalin to adrenochrome in the brain. Factors which facilitate formation of NAD from tryptophan and B_3 supplements will be therapeutic.

Epidemiology

The first modern description of schizophrenia was written about 1800. It was recognized as being different from manic-depressive psychosis over 100 years ago and termed dementia praecox. Bleuler named it schizophrenia in his classic book written about 100 years ago and when this book was translated into English about 1940 the name became much more common and now we are stuck with it. I write "stuck" because of the enormous stigma and shame to victims and their families.

There is no doubt that it has a powerful genetic background. Twin studies have established this. This has been a mixed blessing, for many believe that once something is labeled genetic it becomes untreatable. It is uniformly distributed around the earth. The estimates vary but it is generally around 1 per cent of the total population who will have one or more episodes of schizophrenia during their lifetime; in some areas and in some societies it is much more common. I do not think we really know how prevalent it is. Not every person who has or had it has been diagnosed and counted. There are many who have had short-lived episodes, which have been called depression, anxiety or borderline personality disorder. Early statistics were based upon the number of patients admitted to mental hospitals. In spite of these major uncertainties I think it is much more common than is commonly accepted and will appear in about 2% or more of any population.

Schizophrenic genes are good genes. Dr. David Horrobin[20] was convinced that the introduction of the schizophrenic genes into our genetic configuration was largely responsible for the creation of our modern society. Schizophrenic genes could not have survived millions of years of evolution unless they conferred some evolutionary advantage[21] and they do but only in the relatives of patients who are not sick. There is no advantage in being sick and society usually treated these unfortunate patients so badly that they could not possibly have had any evolutionary advantage. If a person becomes schizophrenic at age 45 and until then has been normally productive and creative, surely that means that there was really not much wrong with their genes but that some long term environmental trigger factors are responsible. It means that these genes which have been normal for 45 years no longer are able to obtain the nutrients they must have in their environment in order to remain well.

The Evolutionary Advantages of Having Schizophrenic Genes

Schizophrenic patients before they become sick and after they recover have many physical and psychological advantages. Physically they are, in general, more attractive, they age more gracefully. Their hair does not gray as fast. They can better withstand severe pain. They become arthritic less often and they have cancer much less frequently and when they do get cancer, they recover. Out of my series of over 5,000 schizophrenic patients and over 1,400 cancer cases I have treated since 1955 only ten had both. They all recovered with orthomolecular treatment combined with standard treatment for their cancer.[22] Schizophrenic patients' first order rela-

tives also are protected against cancer but not to the same degree. I have seen many families with many cases of cancer and very few schizophrenics and other families with many schizophrenic members and hardly any cases of cancer.

Psychologically, those with schizophrenia are more creative and enterprising. They tend to see relationships in the world that the rest of us do not see. The LSD experience has a similar effect; many years ago we studied the psychedelic reaction as a way of enhancing creativity. Many brilliant writers, poets, artists, even Nobel Laureates had these good genes,

Possessors of the schizophrenic good genes have an evolutionary advantage but they have to be fed properly. They need vitamin B_3, relief from oxidation conditions in the body and increased use of antioxidants.

The Clinical Picture

Schizophrenia is characterized by a combination of perceptual changes and thought disorder which may lead to strange or psychotic behaviour. But when well, either before they become sick or after they have recovered, they do posses several advantages, both physical and psychological. If this syndrome is caused by hyperoxidation of the catecholamines leading to increased production of adrenochrome and similar chrome indoles, then it should be possible as an intellectual exercise to predict what the syndrome will be like, simply by knowing the properties of adrenalin and adrenochrome. A student of these compounds from Mars visiting earth should anticipate what is the schizophrenic syndrome.

Adrenochrome has the following properties and each one should lead to consequences:

1) A neurotransmitter inhibitor. Perceptual changes and thought disorder. True for schizophrenia.

2) A mitotic inhibitor. Interference with growth if first occurs in children. Decreased incidence of cancer and better response of the cancer to treatment. True.

3) Toxic to heart muscle. Increased incidence of cardiac disease. True.

4) Formation of melanin pigments. Skin changes in pellagra and in some schizophrenic patients. True.

5) Patients made worse by oxidative stress. True.

6) Antioxidants therapeutic. True

Summary

Schizophrenia can be triggered by factors which increase oxidative stress. Conversely, antioxidants and decreased stress will be therapeutic. Schizophrenia is characterized by changes due to sensory misinterpretations of afferent stimuli and inability to judge that these changes are not true.

Psychotic behaviour is comprehensible if one determines the perceptual distortions.

Adrenochrome and similar compounds in common with the hallucinogens cause these perceptual changes.

Vitamin B_3 is required to prevent excessive oxidation of adrenalin to adrenochrome in the brain. Factors which facilitate formation of NAD from tryptophan and B_3 supplements will be therapeutic.

Possessors of the schizophrenic good genes have an evolutionary advantage but they have to be fed properly, they need vitamin B_3, relief from oxidation conditions in the body and increased use of antioxidants.

Conclusion

In 1960 Dr. Osmond and I suggested the following criteria for a good hypothesis[23] . First: It must account both inclusively and economically for what is known already; an hypothesis, which fails to do this, would be automatically disqualified.

Second: It must do this better than any previous hypothesis. Third: It must be testable in a way which will readily lead to its refutation should it be false, using methods available to science under scrutiny. Is there any reason why psychiatry should require anything different from the rest of science? It should also be useful in directing research into productive areas.

I think our adrenochrome hypothesis meets all these criteria. It does take into account most of the clinical findings in schizophrenic patients but of course cannot account for the large number of biochemical findings that are being discovered. It takes into account clinical findings but cannot be compared to any previous hypothesis, as there have been none as inclusive and comprehensive as this. The purely psychological hypotheses of schizophrenia have been dismal failures and have hurt many patients and their families. Biochemical hypotheses have been crude and have not led anywhere. It is testable but unfortunately psychiatry has been too preoccupied with drugs and the minutiae of how they work that no attempt has been made to do so and finally it has lead to the treatment of schizophrenia using orthomolecular methods which are much more successful than using only drugs. Thousands of productive schizophrenic patients are normal.

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