Diagnosing The Schizophrenias

David R. Hawkins, M.D.I

I. DEFINITION

A. Although the term schizophrenia has been in use for 75 years, the definition of schizophrenia is still a matter of discussion and scientific inquiry. In addition to scientific confusion about the exact meaning of the term, the lay public has further misunderstandings about the meaning of the term, and it is a popular misconception that it denotes a "split personality."

Bleuler originally meant by the term that there is a split between feeling and thought and that this was a hallmark of the illness which he characterized as one that did not necessarily lead to dementia as Kraepelin had thought with his term dementia praecox, but instead was identified with four basic characteristics, these being: autism, ambivalence, a loosening of associations, and affective defect. Since that time, there have been many additions and elaborations of the term and many subclassifications offered, many of them oriented towards the clinical course or observational depictions of the various clinical appearances of the illness at various stages. For many

Medical Director, The North Nassau Mental Health Center, 1691 Northern Boulevard, Manhasset, L.I., N.Y. 11030. **This paper was presented at the Fifth Annual Meeting of the Canadian Schizophrenia Foundation in Winnipeg, Manitoba, June 5 - 6, 1976.**

years, the diagnostic and statistical manuals listed the primary types of schizophrenia as simple, hebephrenic, paranoid, and catatonic. This was later elaborated into acute and chronic, or reactive and process. Scandinavian workers added the term "schizophreniform psychosis." Hoch and Polatin described pseudoneurotic schizophrenia, and recently the most commonly made diagnosis is that of schizophrenia, chronic undifferentiated type.

Definitions of the disease have, of course, been based upon the orientation of the authors as to the basic etiology of schizophrenia as is, for example, implied by the term, schizophrenic reaction. To add to the confusion it has been questioned whether schizophrenia or mental illness, for that matter, is a disease or just a myth, according to Szasz. Labeling theorists (Murphy, 1976) have questioned whether or not it is just a sociologically inspired label, and Ronald Laing has pictured it as an atypical lifestyle and reaction to a sick society.

Crosscultural studies have brought to our attention that schizophrenia is diagnosed more frequently in the United States than it is in Britain or Europe (Hawk et al., 1975), and it has been inferred that under the right circumstances even normal people masquerading

as mental patients may be mistakenly diagnosed as schizophrenic when they were in fact merely malingering. Attempts have been made to classify schizophrenia based on the occurrence of certain constellations of symptoms such as Schneider's first- and second-rank symptoms, and computers are now being used in classifications of schizophrenia based on symptom clusters (Carpenter and Strauss, 1974).

The various definitions of schizophrenia, in reality, are not in conflict with each other, but represent different points of view at various points in time and represent the expansion of knowledge which derives from continued study and investigation of this complex disorder.

In Orthomolecular psychiatry we refer to the schizophrenias, and by the use of the plural, we emphasize the biochemical differences which exist in various groups of patients which are of significance from a practical and therapeutic, pragmatic viewpoint.

B. Genetic Studies

Some of the confusion about whether or not schizophrenia is a valid entity has been solved by genetic studies of schizophrenia and, of these, the twin studies have been the most often discussed in providing definite scientific proof of the validity of the concept (Kety, 1976). Since at least 1928, published twin studies have consistently shown a much higher incidence of schizophrenia in monozygotic twins of patients having the disorder than amongst dizygotic twins in whom the disorder has shown approximately the same frequency as would be expected in siblings. The studies show a concordance rate of between 40 and 60 percent for monozygotic twins and a concordance rate of about 10 to 15 percent for dizygotic (fraternal) twins. Despite the conformity of the data, for many years it was argued that the high concordance rate was due to the fact that there were strong genetic factors in at least some forms of this illness which would, therefore, appear to be a valid disease entity. Genetic studies also demonstrate a significant concentration of the illness in the biologic relatives of schizophrenics who are reared in different environments, further emphasizing the importance of genetic over environmental factors. Other cross-cultural studies reveal that the illness appears in all cultures in approximately the same frequency independent of the marked difference in environment.

The twin studies have been the subject of much comment in psychiatry and, from the Orthomolecular view, I would like to make some additional ones. The first question is why the concordance rate amongst identical twins is not 100 percent? This has led to the conjecture that environment plays a decisive role as well as heredity. Several things can be said. Firstly, these studies were based on clinical observation; in other words, the concordance rate was based upon the appearance of overt schizophrenic illness in one of the twins, and were the studies to be redone using more subtle criteria such as scores on the HOD test, the concordance rate would be higher. Roger Williams has pointed out that so-called identical twins are not really identical and when studied biochemically show great variations. For instance, identical litter mates of guinea pigs may show 15 times the requirement for ascorbic acid as another litter mate. I suspect the genetic factor would become more obvious under experimental conditions. For instance, we have seen a twin with schizophrenia which did not become manifest until the patient went on a crash diet accompanied by the use of amphetamine-containing weight reduction pills. In another instance, the biologic predisposition in the identical twin did not become apparent until the patient took hallucinogenic drugs which precipitated an overt schizophrenic illness. Therefore, in counseling twins as schizophrenic patients, we advise them to avoid all the factors that are known to precipitate the illness, such as crash diets, use of amphetamines, strong hallucinogens, failure to correct hypoglycemia, etc.

The Nature-Nurture controversy has finally been resolved by the NIMH Danish Adoptee Studies of Wender et al., 1976, which showed that borderline schizophrenia is wholly genetically determined and that, in fact, environment plays no demonstrable role in its development.

In summary, then, we can say that the use of the term schizophrenia is a valid one from a medical viewpoint. It denotes an illness with a very strong genetic component, and when the illness does not appear when it might be expected, it is because of the presence or absence of known precipitating factors in biologically susceptible individuals. Discussions of genetic studies usually conclude with the fact that there are as yet unknown environmental factors which play an important part in this illness. By this it is usually inferred that environmental means cultural, familial, or psychological factors. However, I think more important than these are the constituents of the biologic environment and, most specifically, as Roger Williams has pointed out (1975), the biologic environment of the patient's cells. Therefore, it is most probably the molecular environment of the patient's cells which determines whether or not the genetic factors will become manifest as overt, clinical schizophrenia.

C. The term "schizophrenia" as used in Orthomolecular psychiatry

We view schizophrenia as basically a biologic illness which occurs in genetically predisposed individuals under certain environmental conditions, and by environmental we mean molecular environment of the patient's cells. I believe that psychological factors play a role, not because of the content of the psychological factors, but because of their biochemical consequences in changing the molecular environment of the brain cells.

II. THE DIAGNOSTIC PROCESS AND PROCEDURES

A. Introduction

Schizophrenia is characterized by variability and diversity (Van der Velde, 1976). Its manifestations are complex, diffuse, and changeable and differ not only amongst individuals, but in the same individual at different times, at different ages, and under different circumstances. In the book **Orthomolecular Psychiatry** which I edited with Dr. Pauling (1973), I pointed out that schizophrenia is a disease process which, if undetected and allowed to progress, may lead to psychosis and irrationality, but that neither psychosis nor irrationality is necessary to the diagnosis of the illness. With this view we differ considerably from the rest of psychiatry as it is practiced currently, in that we pick up earlier and subtler manifestations of the illness before they become grossly observable.

Thus, we view the usual diagnostic criteria for schizophrenia to be late manifestations of the illness. As an illustration, tuberculosis used to be diagnosed by bloody sputum, fatigue, exhaustion, weight loss, the sounds of cavity formation in the lungs when the chest was listened to with a stethoscope. Then, with the advent of x-ray, the illness was diagnosed before the development of any of these late manifestations, and with the development of immunologic techniques, an infection could be diagnosed before it even showed up on x-ray. Thus, as scientific knowledge progresses, and the more we know about a disease, illnesses are diagnosed at an earlier and earlier stage which is of considerable importance. It is obviously better and easier to treat an illness in its very earliest stages before it has done damage to the patient and his life has been affected detrimentally.

As I have described elsewhere (Hawkins and Pauling, 1973), schizophrenia begins as subtle, subjective changes associated with perceptual changes. These earliest manifestations are usually not observable and may not be reported by the patient, nor even recognized as abnormalities. Because the illness occurs most typically during adolescence, the adolescent has not lived long enough to establish norms for feeling and perception and often the parent merely concludes that these changes are due to growing older and are just normal for him or her.

B. Patient's History

Patient's description of the onset of the illness is so variable that no generalized description can be made that is really satisfactory. It is generally known that the onset of schizophrenia is usually considerably different clinically than that described in a textbook.

The subject of an important paper by Drs. John Varsamis and John Adamson from the University of Manitoba who recently wrote in the **Canadian Psychiatric Association Journal** (1976) is that the onset of schizophrenia is characterized by perceptual changes manifesting themselves as physical symptoms. They notice that before the onset of the schizophrenic illness at least 50 percent of patients have visited their family physicians complaining of weakness, backaches, fatigue, and similar type symptoms. They selected 64 patients and tabulated their prodromal complaints and found that 86 percent had complained of weakness, *22* percent had complained of incoordination, 48 percent complained of physical pain such as headaches, backaches, abdominal pains, or pains in the extremities, 17 percent had altered cutaneous sensations, 39 percent had physical symptoms relating to altered autonomic nervous system functions such as gastrointestinal or urinary disturbances, profuse sweating, fainting, and other cardiovascular symptoms, 47 percent had other physical symptoms for which there was no physical basis. In addition, 49 percent had alterations of hearing in the form of hallucinations, 9 percent had visual hallucinations, and 20 percent had altered perceptions of taste or smell. Thus, the typical patient's illness began with weakness, he frequently had a defective sense of balance, complained of incoordination, had pains in the head, chest or abdomen, arms or legs, skin sensations of tingling or numbness, heat or cold or vibration, often urinary frequency, gastrointestinal symptoms such as nausea, vomiting, and diarrhea, often had flushing and palpitations. They noted correlations between certain sets of symptoms. For instance, if the patient had marked fatigue he or she often socially withdrew; if the patient had hallucinations of taste of smell, he or she often had delusions of being poisoned or gassed.

This is a very important study in that it validates many of, the statements and findings of Orthomolecular psychiatrists over the years. It also points out the importance of using the HOD test in everyday medical practice in that 50 percent of the patients had consulted medical practitioners prior to the onset of the psychosis, and the HOD test would have picked up the altered perceptions which precede the more obvious clinical manifestations of the illness. Both Dr. Green and Dr. Kowalson, medical practitioners in Canada, have written of the importance of using the HOD test (1975). Dr. Kowalson termed patients who had elevated HOD scores as having metabolic dysperception, and Dr. Green has written about detecting the early onset of the illness when it would still be best described as subclinical pellagra, especially in children (1975).

There are many excellent and brilliant descriptions of patients' subjective experiences with the onset of their illness and currently the book, **East of Eden,** by Mark Vonnegut, is one of the best known. The book, **In Search of Sanity,** by Gregory Stefan was the first lengthy description by such a patient who was eventually helped through Orthomolecular psychia-

try. Depression is probably the most common psychiatric symptom we see as a presenting symptom in patients. I would list anxiety and insomnia as two other very common symptoms, followed in frequency by complaints of difficulty in either functioning or adjustment with family or home school or job.

C. Observation and Interview

In observing and interviewing the patient, Orthomolecular psychiatrists look for subtle alterations of perception. These result in alterations and disturbances of body image so that the patient may be inordinately concerned about various body parts. He feels that they are somehow disconnected or too large, and we have already enumerated the many somatic complaints which may accompany these changes. The patient's gait and posture may indicate an altered proprioceptive sense so that there is a lack of grace and spontaneity in animal movement. Patients may have a variety of visual complaints, usually not of images but of spots, lines, wavy figures which they see out of the corner of their eyes. They may become hypersensitive to light. Other people's faces may become distorted. There may be auditory hypersensitivity and a withdrawal from an environment where there is a lot of conversation; patients become easily confused by sensory input and withdraw from crowds and social situations. There may be alterations of space and smell which may have gone on to delusions in an attempt to explain their occurrence. The patient may respond by numbed withdrawal, by depression, or by elation, and there are often reports of altered thought processes, the most common complaints being that of confusion, or of thoughts coming too fast so that the patient complains of having a racing mind. All of these symptoms lead, of course, to impairment of functioning in various areas, and it is the impaired functioning which often brings either the patient or the family to seek help.

D. Psychological Test

We test for these alterations in perception by use of the HOD, EWI, Green Test for Perceptual Malfunctioning in Children, the OIT. In addition, we may use a routine psychological battery, including the MMPI, Rorschach, Thematic Apperception Test, and Draw-A-Per-son or Bender Gestalt. The administration of the perceptual test is often the first chance the patient has had to reveal the extent and nature of this illness to others, as many of his symptoms have been difficult to explain to others. Details of the use of the HOD test in clinical practice are described in a new book on the Hoffer-Osmond Diagnostic Test published by Krieger Publishing (1975).

In my view, the failure to use tests for perceptual functioning is probably the biggest deficit in all the research that is now going on in the field of schizophrenia.

E. Laboratory Tests*

The glucose-tolerance test is one of the most important diagnostic procedures, and in doing this test we also do insulin levels to detect reactive hypoglycemia which is present in a large percentage of psychiatric patients. We have seen many patients in whom the correction of hypoglycemia corrected the entire mental disorder and eliminated all the patient's symptoms (Yaryura-Tobias and Neziroglu, 1975; Yaryura-Tobias and Neziroglu, 1975a). In other patients, although the laboratory indicates severe hypoglycemia, it seems to be of little clinical importance. There are many patients who only become psychotic when their blood sugars drop precipitously, and a sugar-free diet makes the difference between success and failure in their treatment. In other patients, the hypoglycemia increases the severity of their illness or contributes heavily to symptom formation. For instance, a patient may have, primarily, paranoia and depression. Correction of the hypoglycemia may eliminate the depression, but not the paranoia. Thus, it plays a

* In addition to the routine lab work consisting of CBC, urinalysis, computerized chemical profiles for electrolytes, liver function and kidney function, uric acid level, and muscle enzymes.

variable part from patient to patient and in the same patient, at different times.

Thyroid Tests: We routinely do tests for thyroid function for several reasons: to rule out hypo-or hyperthyroidism masquerading as schizophrenia, which occurs occasionally; another reason is that we wish to establish that the patient has normal thyroid function because we may want to use thyroid extract later on in the patient's treatment.

EEG: We routinely do an EEG on all our patients, not only to rule out organic brain disease or a convulsive disorder, but to pick up certain EEC patterns correlated with certain types of behavior syndromes. Dr. Yaryura-Tobias has described a triad of cerebral dysrhythmia associated with hypoglycemia and violent behavior for which the treatment is specific, consisting of a sugar-free diet, Dilantin, and vitamin B6 (1975a).

Folic Acid and B12 Levels: We routinely test for these as they often show a deficiency as has been reported over the years in the psychiatric literature, and most recently Dr. Newbold has written a book showing the values of B12 in the treatment of a variety of psychiatric disorders, especially schizophrenia (1975).

Mauve Test: We routinely do the mauve test to pick up those patients who were first described by Hoffer and Osmond as malvarians. This work was later elaborated on by Irvine (1973), Sohler (1973) (cited in Pfeiffer, 1975), and Pfeiffer (1975). Elevated mauve levels have their definite significance for diagnosis and treatment and may indicate the Sara Syndrome as described by Pfeiffer. These are subtypes of schizophrenia in which histamine levels are normal, but the patient puts out excessive amounts of kryptopyrrole in the urine, thereby ending up with a B6 and zinc deficiency. This zinc and B6 deficiency may result in abnormal EEG, typified by occasional slow waves and isolated high voltage spikes. Dr. Pfeiffer calls such patients pyrolurics who are characterized by having better affect, white spots on their fingernails, loss of dreaming, sweetish breath odor and, occasionally, abdominal pain in the left upper quadrant. These patients may also have stretch marks, inability to tan, sensitivity to sunlight and possible tremors, spasms or amnesia. There may be sexual impotency and intolerance to barbiturates as well as menstrual irregularities and anemia, which does not respond to iron, but does respond to vitamin B6. Their blood counts may show an eosmophilia *up* to 20 percent. In his book, **Mental and Elemental Nutrients,** Dr. Pfeiffer describes the successful treatment of over 400 cases of this syndrome with high doses of B6 and zinc, and he thinks that both Emily Dickinson and Charles Darwin were good examples of this syndrome.

Histamine Levels: Patients with excessive mauve factor in the urine account for about 30 percent of the patients, and patients with abnormal histamine levels constitute another 70 percent. Fifty percent of the patients are classified as histapenia, meaning they have abnormally low histamines. These patients are characterized as having over-stimulated, overactive thought processes, severe dysperception in many areas, frequent hallucinations, insomnia, and a high threshold for pain. They show high-serum copper levels, and high copper destroys histamine. This has important treatment significance, as these patients do well on niacin, vitamin C, B12, and folic acid. The 20 percent of patients who have elevated histamine levels are termed-histadelic, characterized by suicidal depression and obsessive-compulsive symptoms, and may have a "blank mind." They seldom suffer hallucinations or paranoia. Discovery of the high histamine is important for treatment which, for these patients, consists of Dilantin, calcium, antihistamines, methionine, plus trace metal supplements.

Hair Tests: The hair test is utilized to test for trace elements, and they reflect the elevated copper levels as well as other correctable abnormalities. In addition, we look for heavy metal

contamination such as lead or mercury poisoning. Elevated mercury levels may result from accidental exposure, or may be occupational. Elevated blood levels are more common, and Dr. Cott has reported a high incidence of elevated lead levels in city children, presumably from auto exhaust.

Biogenic Amine and Catecholamine Profile: We are now doing blood levels of the biogenic amine and catecholamines, including serotonin, dopamine, adrenaline, and noradrenaline, and the urinary metabolites of MHPG, SHIA, UMA, and PEA. We hope, thereby, to gain further useful knowledge of additional subtypes of schizophrenia.

Cerebral Allergy Testing: Cerebral allergy is a relatively new concept in psychiatry (Randolph, 1966, 1970). Its presence may be suspected from the patient's history, and it constitutes a whole separate area of investigation. It may be tested for by direct sublingual provocative food testing in which the patient's reactions and pulse rates to varied solutions of common food allergens are recorded. These allergies may also be detected by elimination diets, or rotational diets, or environmental isolation from suspected offending agents. In this connection, wheat allergy is most often detected, and recent scientific reports demonstrate that gluten-free diets are beneficial to unselected populations of schizophrenics. This work has been validated to such a degree (Singh, 1976), that at Brunswick Hospital all patients are initially placed on a gluten-free as well as a sugar-free diet. There is genetic evidence linking celiac disease, which is characterized by gluten intolerance, with schizophrenia, and there is also much evidence indicating wheat intolerance in schizophrenics. In addition to food allergy, there are many other contact and inhalant allergens capable of producing emotional and perceptual changes in susceptible patients. Of the various chemicals, the petrochemicals which are petroleum derivatives are the most common offending agents.

III. SUMMARY AND CORRELATION OF DIAGNOSTIC STUDIES

A complete diagnostic evaluation and treatment, therefore, consists of taking both the family and patient's history, a period of observation, a diagnostic interview, comprehensive psychological testing, including perceptual testing with at least the HOD, EWI, automated MMPI, or Green Test for perceptual dysfunction in children, a comprehensive chemical profile which includes tests for electrolytes balance, liver function, and creatine and uric acid levels, urinalysis, complete blood count, EEG, urine test for mauve factor, test for thyroid function consisting of T-3 and T-4 or ETR, histamine level, insulin levels, five- or six-hour glucose-tolerance test, folate and B12 levels, biogenic amines and catecholamine profile, hair test for trace metals, serum copper levels, and cerebral allergy tests. For those patients who are hospitalized, in addition, we obtain skull x-rays, neurological and physical examinations and, when indicated, specialized tests such as NAD level, tests for galactose intolerance, salt dumping syndrome, etc.

From all of the above data, we have the information we need to more effectively diagnose the patient's subtype of schizophrenia and devise a treatment regimen based upon his individual biological characteristics. By using all of the above, we hope we can detect schizophrenia in its earlier and more subtle stages when it is easier to treat and before it has reached a more advanced stage. The treatment of many of these subtypes of schizophrenia is specific, and I will enumerate some of them.

There is a type of schizophrenia which only occurs in patients who have been drinking alcoholic beverages, usually to excess. This is frequently accompanied by hypoglycemia, which may have preceded the onset of the heavy drinking. The schizophrenic symptoms are only present if the patient has been recently drinking. According to the work of Randolph and others, this may be due to corn allergy or allergy to other grains

or potatoes from which the alcohol is made. In other patients, it is the hypoglycemia resulting from the alcohol ingestion that triggers the overt schizophrenic symptoms. Some patients have progressed to actual alcohol addiction, and their schizophrenia clears only when they are able to achieve sobriety.

There is a distinct type of schizophrenia known as chronic, relapsing catatonia, which demonstrates shifts of nitrogen balance and where high-dosage thyroid is curative. There are other patients who have hypothyroidism who are admitted for treatment with a tentative diagnosis of schizophrenia. In these patients, low-dose thyroid is curative. There are occasional patients with hyperthyroidism who present themselves in an agitated state and have been misdiagnosed as schizophrenic. There are many patients who develop a schizophrenic syndrome in response to cerebral allergy which may be due to environmental chemicals or, more commonly, foodstuffs. There are subgroups of schizophrenia classified as histadelic, histapenic, and pyroluric (Sara Syndrome) in which correction of abnormal histamine levels, spermine, or sperma-dine is curative, or in whom B6 and zinc is curative. Some patients present a triad of hypoglycemia, cerebral dysrhythmia, and violent behavior which is intractable and does not respond to any treatment except Dilantin, B6, and the hypoglycemic diet. There are many patients with subclinical pellagra for whom merely high doses of megavitamins are curative. There are patients with hypochondriasis and numerous somatic complaints who show elevated HOD scores and who may be better diagnosed as metabolic dysperception. There are many patients who have a wheat sensitivity and who respond well to gluten-free diets. Some present a picture of paranoid schizophrenia, and HOD tests and others indicate the likelihood of a Folie A Deux which is further discovered by the history taking. There are patients who have an L-dopa-pre-cipitated schizophrenic syndrome which is antidoted by B6 as well as removal of the L-dopa. There are cerebral syndromes which appear as schizophrenic psychosis due to toxic and heavy metal poisoning which is picked up by the hair tests, and some patients have to be detoxified from copper, lead, or mercury. Lastly, a comprehensive diagnostic work-up also allows us to differentiate the schizophrenic syndrome from reactive psychosis, hysterical psychosis, and manic-depressive psychosis. This is important as many patients formerly diagnosed as acute schizophrenic reaction have been found to be responsive to lithium and are now being reclassified as manic-depressive illness.

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