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Abstract

Dr. Abram Hoffer and Dr. Humphrey Osmond have formulated a biochemical theory of schizophrenia based on a defective adrenal metabolism which results in the production of neurotoxins in the schizophrenic's body. They have also developed a therapy for schizophrenia consisting of massive daily doses of Vitamin B-3 (nicotinic acid) and other supplements. They detect schizophrenia by means of a chemical test (paper chromatography) and a psychological test (the Hoffer- Osmond Diagnostic test).

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The schizophrenia research of Hoffer and Osmond was largely the result of two factors. First was the need for a medical basis for the etiology and specific treatment of schizophrenia. Traditionally psychiatrists have viewed schizophrenia as a severe emotional disorder resulting from early psychic trauma or moral conflicts. Treatment consisted of intense psychotherapy which usually proved futile. In the course of therapy, the patient usually became worse and worse while the psychiatrist became richer and richer. The second factor was largely an outgrowth of this trend in psychiatry. Numerous myths grew up around schizophrenia. Some psychiatrists support the myth that diagnosis of schizophrenia is not important and that it is necessary to concentrate only on personality. This resulted in an antimedical approach to the treatment of this disease. A second myth is that schizophrenia is caused by something being wrong in the personality. Many diseases, including the general pareses, went through this stage. A third myth is that schizophrenia is due to poor mothering. Hoffer and Osmond feel that this view has not been supported by research. They think many mothers today suffer needless feelings of guilt because their children's illnesses are related to too early or too harsh toilet training, quarreling

at the breakfast table, or inconsistent discipline. In short, Hoffer and Osmond have taken a dim view of the Freudian approach to schizophrenia (Hoffer & Osmond, 1966, pp. 4-5).

Adrenochrome - adrenolutin Hypothesis

The adrenochrome -adrenolutin theory of schizophrenia was first developed publicly in 1952. It involved the study of biochemical products of the adrenal glands, two small triangular-shaped organs weighing only one ounce each, one of which sits on top of each kidney. The cells of the adrenal medulla convert tyrosine, a simple amino acid, into noradrenaline and adrenaline. When an individual is threatened, noradrenaline is converted into adrenaline which flows from the adrenal medulla through the adrenal cortex and into the bloodstream, where it is carried to all parts of the body. In an emergency situation, adrenaline acts as a coordinator of the many mechanisms required for protection of the organism from the impending danger. The entire body is almost instantly mobilized for fight or flight. The breathing rate increases, the heart rate goes up, blood pressure increases, sugar is poured into the blood, and blood is channeled from the internal organs to the muscles which are needed for defense. Thus the subject is able to use a large energy reserve over a short period of time.

Once the threatening situation is over and the individual has relaxed, the excess adrenaline is converted into a very toxic and changeable hormone called adrenochrome. If a water

solution of adrenaline is allowed to stand in the open air, some adrenochrome will be formed, giving the solution a reddish tinge. Since adrenochrome is toxic, it must be removed from the body along with any excess adrenaline. Normally the body accomplishes this by converting the adrenochrome into 5,6, dihydroxy-N-methyl-indole (also known as dihydroxyindole or leuco-adrenochrome), which is harmless to the body and can be excreted by the kidneys. Dihydroxyindole acts to counteract the anxiety--producing effects of adrenaline, and the anxiety level of the individual depends on the equilibrium between adrenaline and dihydroxyindole at any given time.

For some unknown reason, the schizophrenic's body converts adrenochrome into adrenolutin, a potent neurotoxin which interferes with normal chemical reactions in the brain. The process of schizophrenia is then underway. This whole process from adrenaline to adrenochrome to dihydroxyindole or adrenolutin is the essence of the adrenochrome - adrenolutin theory of schizophrenia (see Figure 1). (Hoffer & Osmond, 1966, pp. 50-53).

Because of the disproportionately high incidence of schizophrenia in the family background of schizophrenics, many investigators have concluded that genetic factors play a key role in the incidence of schizophrenia. Huxley, Mayr, Osmond, and Hoffer have concluded that, in the great majority of cases, schizophrenia is based on a single partially dominant gene with low penetrance (25%). In separate studies, Huxley and Mayr independently concluded that it involved a genetic morphism. Evolutionary geneticists now agree that all genetic characters

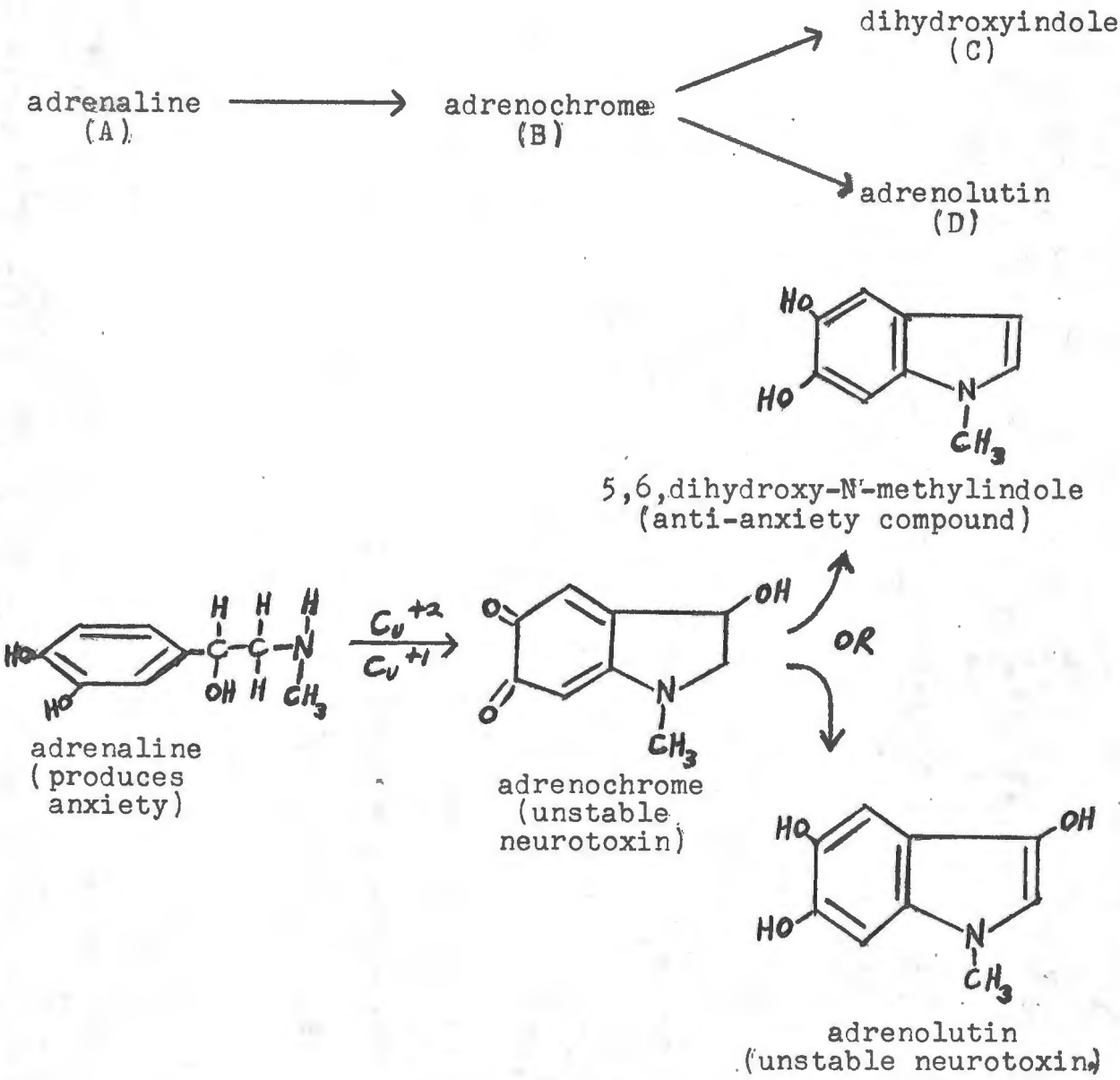

Figure 1. Biochemical Scheme for Adrenochrome-adrenolutin Hypothesis (Hoffer & Osmond, 1966, p. 53; DiPalma, 1965, pp. 329, 465).

which exist in a population at a higher frequency than can be maintained by mutation alone involve morphism.

The abundant evidence of a strong genetic component in schizophrenia included the following. (a) Only certain children in a given family became schizophrenic. (b) Monozygotic twin-pairs showed a concordance rate of 76-91%, while dizygotic pairs had only a 10-17% concordance rate. (c) The incidence of manifest schizophrenia is approximately 1 % in all racial and ethnic types and probably in all social classes. (d) An examination of schizophrenics and normal siblings of the same sex and less than two years' difference in age, whose mothers were not schizophrenic, showed that the future schizophrenics and their siblings manifested marked personality and temperament differences from an early age, and that these could not be associated with environmental influences, including psychological trauma. The future schizophrenics were more dependent and less able to deal with traumatic events: they were schizoprone apparently from birth.

However, schizophrenics have certain physiological advantages over normal individuals which somewhat compensate for the mental disruption of their illness. Overt schizophrenics are extremely resistant to surgical and wound shock and recover much more rapidly than normal patients. They are also extremely resistant to visceral perforation, to high doses of histamine (correlated with fever mast cells in the skin), to insulin,

thyroxin and other physiologically active substances, to pain, to arthritis, to many allergies, and probably to many infections. Osmond has seen a schizophrenic recover successfully from the most appalling burns which would have killed a normal person in hours or minutes. (Huxley, Mayr, Osmond, & Hoffer, 1964, pp. 220-221).

The unique characteristics of the schizophrenic can be accounted for by the adrenochrome-adrenolutin theory. The rare occurrences of allergies or arthritis in schizophrenics as well as their high resistance to histamine may be due to the presence of adrenochrome, an anti-histamine nearly as powerful as some of the weaker commercially made anti-histamines. Small quantities of adrenochrome constantly present in the body could protect schizophrenics against allergies more effectively than larger doses taken orally by non-schizophrenics at intervals. The constant presence of adrenochrome may also account for the schizophrenic's remarkable resistance to medical and surgical shock (Hoffer & Osmond, 1966, p.93).

Schizophrenics seldom have diabetes. Adrenochrome and adrenolutin block the action of insulinase, the enzyme which destroys insulin in the bloodstream. Therefore, the schizophrenic has sufficient insulin to control the sugar level in his blood.

If schizophrenia comes on early in life, it prevents normal growth and development. The victims tend to be slender,

slight, and too narrow in the chest from front to back. In severe cases the halves of the body develop differently, producing asymmetrical features. Long before adrenochrome was suspected of being related to schizophrenia, it was known to be a very powerful inhibitor of cell division, a cell mitosis poison. Therefore, adrenochrome could also interfere with other body processes which depend upon the rapid growth of tissues. Schizophrenics have a low resistance to tuberculosis, probably because adrenochrome prevents fibrous tissue from encasing the tubercular lesions in their lungs. They also sometimes show a reduced growth of hair and nails, as well as a defective formation of sperms.

Schizophrenic patients are prone to develop scurvy, a condition resulting from a deficiency of vitamin C (ascorbic acid) in the body. Adrenochrome combines chemically with vitamin C and uses it up quickly, leaving a deficiency in the schizophrenic. Briggs has shown that when scurvy is artificially induced in guinea pigs, they excrete certain unusual compounds in their urine. He has also shown that patients who have schizophrenia excrete the same substances.

During normal brain functioning, gamma amino butyric acid (GABA) regulates the transmission of impulses across neural synapses. GABA is made from the amino acid, glutamic acid, by the loss of one molecule of carbon dioxide. The enzyme which makes it is prevented from doing so by adrenochrome.

Thus, when adrenochrome is present, there will be a deficiency of GABA and the brain, agitated by an over-abundance of stimuli, will be too excitable or irritable. This could account for the fact that the majority of schizophrenic patients are irritable and have abnormal brain wave changes or convulsions.

Adrenochrome also blocks the action of the enzyme which destroys acetylcholine, one of the messenger chemicals that crosses the synapse from the nerve cell to the neuron. An excess of acetylcholine in the synapse will then add to the irritability or excitability of the brain (Hoffer & Osmond, 1966, pp. 91-92).

Adrenolutin will gradually destroy the neurons of the brain and nervous system. The body has only one known way of protecting its vital and irreplacable neural tissues from adrenolutin, which comes from adrenochrome. The blood normally contains a protein called ceruloplasmin. It is a blue copper-containing substance which chemically binds adrenolutin so firmly that it is mopped up from the blood stream and unable to poison the brain and nervous system. During stress when more adrenaline is secreted and converted into adrenochrome and adrenolutin, there is also more ceruloplasmin in the blood.

Because of its ability to remove adrenolutin, ceruloplasmin has been found to play an important role in the recovery of schizophrenics. It is made in the placenta, and during the last three months of pregnancy more is secreted from the placenta into the mother's blood. Thus, nature has provided the mother

and fetus with protection against adrenolutin or adrenochrome. After the baby is born, however, the ceruloplasmin level in the blood rapidly decreases and reaches a normal level in about two weeks. If the woman was schizophrenic before pregnancy, her psychotic symptoms usually return at this time. Melander has shown that ceruloplasmin injections will cure the majority of acute schizophrenics to whom it is given.

Taraxein, the toxic protein isolated from the blood of schizophrenics by Heath and his associates at Tulane, plays an important role in the formation of schizophrenia. Melander believes that taraxein sensitizes the brain to adrenolutin. During their evolutionary history, mammals have developed a chemical blood-brain barrier which keeps toxic substances like adrenochrome and adrenolutin out. Melander believes taraxein lowers this barrier, enabling adrenolutin to penetrate into the brain. Taraxein makes animals and humans peculiarly sensitive to minute quantities of adrenolutin which are otherwise not dangerous (Hoffer & Osmond, 1966, pp. 94-95).

Hoffer and Osmond have induced model psychotic states (similar to those achieved with LSD-25 and mescalin) in normal individuals with adrenochrome. 10 mg. of adrenochrome dissolved under the tongue will produce vivid changes in visual perception. Two hours after taking this dose a research psychiatrist felt that trees were exploding in his field of vision. In another test, Dr. Hoffer experienced distorted vision for two days after

taking sublingual adrenochrome. Objects seemed either larger or smaller than normal. The average schizophrenic might panic at these sensations, feeling that he is losing his mind (Hoffer & Osmond, 1966, p. 105).

Asquith reported that during World War II pinkish adrenaline was used during anaesthesia. After the patients revived they had disturbances including hallucinations. The case of a young man, whom Hoffer and Osmond call Mr. Kovish, helped convince them that they were on the right track. Mr. Kovish, who was in his middle thirties, friendly, intelligent, and with a lively sense of humor, occasionally suffered from asthma, for which he had inhaled adrenaline regularly for ten years. One night in 1956 he found himself without adrenaline, many miles from home, and stopped at a small drug store. The druggist had only one bottle of adrenaline but it was quite discolored. He was hesitant to sell it but Kovish bought it anyway. Kovish sniffed some and started home. While driving later that night he felt extremely alert but had some difficulty in judgment and some bizarre thoughts. His vision was distorted. The road, which was actually very familiar to him, looked strange. He continued to take the impure adrenaline for several weeks and developed a syndrome which led him to believe he was losing his mind. He saw the world as through a distorted glass, became quite anxious and depressive, had compulsive thoughts, began to doubt himself and his sanity, and suffered from insomnia.

He was extremely irritable and could no longer participate in family life. While discussing this with a friend he casually mentioned the adrenaline. His friend, who had read articles on biochemical causes of schizophrenia, encouraged him to seek professional help. Hoffer and Osmond were excited by his story. Outside of a laboratory, unsuspecting and unprepared, a normal man had taken impure adrenaline and as a result had suffered all the classic symptoms of schizophrenia for several weeks. Hoffer and Osmond duplicated his experience in the laboratory and concluded that adrenochrome or adrenolutin produced the classic symptoms of schizophrenia---changes in perception, mood, and thought---- in human volunteers. Their results have been confirmed by research workers in the United States, Germany, Czechoslovakia, Sweden, Russia, Switzerland, and Canada (Hoffer & Osmond, 1966, pp. 54-59).

Schizophrenia may be simply divided into two categories, process and content. Process is the act of being ill, due to a biochemical abnormality in the case of schizophrenia. Content is concerned with the reactive phases of an illness, with hallucinations and delusions and the like in the case of schizophrenia. These are shaped by personality, culture, society, and the host of variables which at any moment in time determine what a person is. For example, in a non-communist country, a paranoid patient may believe that communists are after him, while in Russia or China, he would believe that

capitalists were pursuing him. A patient's food may taste bitter or brassy because adrenolutin has poisoned his nervous system and affected his sense of taste, but he feels he is being poisoned because in our culture a bitter or brassy taste is associated with poison.

The perceptual hypothesis is that those areas of the brain which integrate, stabilize and maintain constancy of sensory perception are changed owing to the adrenolutin biochemical disorder. As a result, the patient's experience of the world is dramatically changed. Since he must rely on his distorted senses in evaluating reality, changes in his personality and behavior must be expected (Hoffer & Osmond, 1967, pp.47-49).

Detecting Schizophrenia

Since adrenolutin can permanently destroy nerve cells, it is essential that schizophrenia be diagnosed and treated as early as possible. Hoffer and Osmond use two tests to detect schizophrenia. First is a chemical test utilizing a paper chromatography technique to detect a mauve factor in the urine of suspected schizophrenics. By operational definition, malvaria is that disease which is present in any human being when he excretes a mauve factor. Second is the Hoffer - Osmond Diagnostic Test (HOD), a simple card sort test designed so that high scores indicate the presence of schizophrenia.

Hoffer and Mahon, using an extraction method of their own,

have shown that certain compounds, separated from fresh samples of urine on paper chromatograms, give a mauve color. This color develops slowly over 30 minutes as a pink area which slowly turns mauve and within an hour has a typical mauve appearance. It then starts to fade and is usually gone within several hours.

An early morning specimen of urine was obtained from each of 850 patients from the surgical, pediatric, and psychiatric wards. All specimens were analysed blind. The procedure was as follows: Early morning urine was adjusted to a pH of 6.7 and extracted three times with equal volumes of pure ether. The pooled ethereal extracts were dried with anhydrous sodium sulphate and filtered. The extract was then evaporated at room temperature and reduced pressure. (The substances are very heat-labile and in earlier studies were destroyed after being heated to 40°C. in a water bath). The aqueous portion remaining was then extracted with pure chloroform. This was dried with anhydrous sodium sulphate and the chloroform solution was run on paper overnight in isopropanol--ammonia water. Next day the dried paper was sprayed with Ehrlich's reagent. The mauve spot appeared at an Rf of 0.83. The color developed slowly (over 30 minutes) as a pink area which turned mauve slowly and was finally typically mauve. It then began to fade and within 3 to 24 hours was gone.

Malvaria was found in 10.5% of normals, 11.9% of normals

under stress, 24.5% of disturbed children, and 41.8% of all psychiatric cases. The incidence of malvaria appears to rise with the severity of the emotional disturbance, as indicated by the fact that the mauve factor was positive in 52.3% of cases clinically diagnosed as schizophrenia. Its occurrence in 50% of cases of carcinoma warrants further study (see Tables I and II) (O'Reilly, Ernest, & Hughes, 1965, pp. 741,744).

Traditionally, the art of psychiatric diagnosis has consisted of knowing which questions to ask as well as how to evaluate the significance of the answers. At its best the technique was rather subjective to say the least. Hoffer and Osmond have developed the HOD test, consisting of 145 questions on cards. The questions covered perceptual, thought, and affect areas of the usual mental status. The HOD test was designed so that schizophrenic patients would more likely find the questions true than false. Other diagnostic groups would find many fewer questions to be true. The cards were shuffled and subjects placed them into a box marked true or false. When the test was completed the numbers from the back of each card (from 1 to 145) placed in the true box were recorded. Four special scores were developed: (a) a depression score (DS) derived from cards which depressive patients would likely find true; (b) a perceptual score (Per S) derived from cards containing questions which dealt with perceptual changes; (c) a paranoid score (PS); and a global weighted total score (TS).

Table I

Incidence of Malvaria (O'Reilly, Ernest, & Hughes, 1965).

Category	Total Numbers	Number Positive	Percentage Positive
Normal adults ..	277	33	11·9
Normal children ..	134	16	11·9
Cancer patients ..	22	11	50
Disturbed children	49	12	24·5
Schizophrenia ..	86	45	52·3
Affective psychosis	127	60	47·24
Organic states ..	28	8	28·6
Personality disorders	37	10	27
Alcoholics	49	18	36·7
Psychoneuroses ..	41	13	31·7
	850	226	26·58

Table II

Incidence of Malvaria (Hoffer, 1967).

	Number tested	Per cent positive
1. Schizophrenia (a) First attack	50	90%
(b) Second and subsequent attack	300	75%
(c) Chronic (ambulant)	300	50%
(d) Chronic (in hospital 5-20 years)	300	40%
(e) Chronic (in hospital 25-35 years)	25	10%
(f) Recovered	100	0
2. Alcoholics, neurotics, depressions, anxiety state, personality problem, behavior disorders	300	25-35%
3. Mongolian idiots (adults)	100	60%
4. Physically ill	300	10%
5. Normals (4 of normal subjects positive were First order relatives of schizophrenics or malvarians)	100	5%
6. First order relatives of malvarians or schizophrenics	100	35%

Because the incidence of mauve factor cuts across all diagnostic groups Hoffer and Osmond developed the operationale term "Malvaria" to label every human who has mauve factor in his urine.

These scores were highly intercorrelated. High scores are abnormal. Normal subjects have very low scores. Nurses usually administered the test to patients and recorded the true cards on a special sheet. Hoffer then scored the sheets and filed them.

For three years a large number of patients examined for malvaria were also given the HOD test. There was a highly significant association between the presence of malvaria and abnormally high HOD scores. The difference in distributions of total HOD scores is greater between malvariacs and non-malvariacs than the difference between diagnosed schizophrenics and non-schizophrenics. In other words, the chemical test divides patients into more divergent groups. This shows that the biochemical test is more closely related to perceptual and other changes measured by the HOD test, and that both the malvaria test and HOD test measure a similar pathological process (see Tables III and IV, and Figure 2). On the basis of the quantitative results of the tests, Hoffer and Osmond recommend treatment for both malvariacs and non-malvariacs who score high on the HOD test, especially the former (Hoffer, 1965, pp. 175-177).

Treating Schizophrenia

There are four ways of reducing the amount of adrenochrome and adrenolutin in the body: (1) To reduce the formation of adrenaline; (2) To reduce the formation of adrenochrome; (3) To

Table III (Hoffer, 1965).

FREQUENCY DISTRIBUTION OF TOTAL SCORES (HOD) OF SCHIZOPHRENIC AND NON-SCHIZOPHRENIC PATIENTS, WITH AND WITHOUT MALVARIA

	0-39	40-79	80-119	120
Malvaria	34	24	16	6
1. Schizophrenic	18	14	13	4
2. Not schizophrenic	16	10	3	2
Not Malvariac	104	27	7	4
3. Schizophrenic	35	13	3	4
4. Not schizophrenic	69	14	4	0

Differences in Distribution

1 vs 2	N.S.
3 vs 4	5% level
1 vs 3	1% level
2 vs 4	1% level

Table IV (Hoffer, 1965).

PERCENTAGE DISTRIBUTION OF TOTAL SCORES (HOD) FOR SCHIZOPHRENIC—NON-SCHIZOPHRENIC PATIENTS AND FOR PATIENTS WITH AND WITHOUT MALVARIA

CRITERION	CLASSIFICATION	NO. OF CASES	0-39	40-79	80-119	120
Clinical	Schizophrenic	104	51	26	15	8
Diagnosis	Non-schizophrenic	118	72	20	6	2
Mauve	Malvaria	80	42.5	30	20	7.5
Test	Not Malvariac	142	73	19	5	3

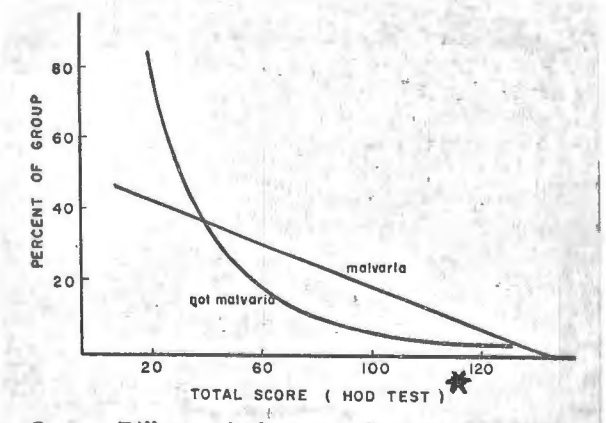

Figure 2. Difference in frequency distribution of HOD total scores between Malvariacs and Non Malvariacs (Hoffer, 1965).

*All scores below 40 are considered normal.

increase the conversion of adrenochrome into beneficial dihydroxyindole;(4) To reduce the concentration of adrenolutin. Treatments have been developed using each technique, and they have improved the recovery rate of schizophrenics.

The production of adrenaline can be reduced only by indirect methods. The patient can avoid anxiety, conflict, and tension-arousing situations as much as possible or drugs can be used to decrease their effect. These include barbiturates and anti-tension compounds such as meprobamate, librium, valium, and the phenothiazine family of tranquilizers. Removal of the adrenal glands is not effective because the body regenerates tissues in other areas of the body which can make adrenaline. Smoking substantially increases adrenaline production due to its nicotine content. For this reason, schizophrenics should not smoke.

The production of adrenochrome can be reduced by removing substances which facilitate the oxidation of adrenaline. Copper ions are usually the culprits involved in the oxidation of adrenaline. Penicillamine can bind copper and remove it from the body. Vitamin C (ascorbic acid) and glutathione, an amino acid, are used with penicillamine to reduce adrenochrome production.

The production of dihydroxyindole, an anti-tension compound which counteracts the effects of adrenaline, can be increased by the use of penicillamine. In the test tube penicillamine combines with adrenochrome and converts most of it into the

dihydroxyindole. Thus, penicillamine has a double function----- to bind and remove copper ions and to convert adrenochrome into the beneficial dihydroxyindole.

Adrenolutin can be removed from the body by injecting ceruloplasmin into the blood. This protein, which is normally present in very slight amounts in the blood, is still a research medicine and is very expensive. This prevents its wide spread use at the present time (Hoffer & Osmond, 1966, pp 61-63).

Thus, the real problem was to find a readily available and inexpensive medication which could prevent the harmful effects of adrenolutin. Hoffer and Osmond reasoned that any chemical which would slow down the formation of adrenaline would, therefore, slow down the production of the toxic adrenochrome and adrenolutin. Nicotinic acid in the body can absorb methyl groups ($-CH_3$) which are needed to convert noradrenaline into adrenaline. Nicotinic acid already had an impressive history as a treatment for several delirious diseases, including pellagra. Pellagra is a vitamin deficiency disease characterized by the three D's: delirium, diarrhea, and dermatitis. The delirium was very similar to schizophrenia. It has been estimated that up to 10% of the admissions to some southern mental hospitals were these pellagra psychotics. When nicotinic acid was added to American flour, this psychosis was all but eliminated.

In May 1952, Hoffer and Osmond began treating their first patient with nicotinic acid. He was a seventeen-year-old boy

admitted to Saskatchewan Hospital in Weyburn with an acute schizophrenic illness which had started only a few days before admission. He was excited, overactive, silly, and at times deluded. He responded poorly to electroconvulsive therapy and was put on deep insulin shock which had to be stopped after less than ten days because of palsy in the right side of his face. Over a three week period his condition deteriorated until he required complete nursing care.

He was started on five grams of nicotinic acid and five grams of ascorbic acid per day, divided into five equal doses. Within twenty-four hours he was improving and ten days later he was described as almost normal. The vitamin therapy was continued for a month, and he was observed for three weeks in the hospital before being discharged to his home. A follow-up three years later showed that he was in good health and had finished his final year of high school. He has remained well and was interviewed as late as June 1964.

Encouraged by this success, Hoffer and Osmond began their first clinical trials of massive doses of niacin and nicotinamide, using a sugar-coated placebo pill with a control group. Thirty schizophrenics from the psychiatric ward of a general hospital were selected and divided into three equal groups at random. One group was started on the placebo, one on niacin, and one on nicotinamide. Neither the patients nor the nursing staff knew which medication the patients were taking. The placebo group

showed the poorest results, being well only half the time for two years after discharge. The niacin and nicotinamide patients remained well most of the time in the two year follow-up period.

Using a larger sample of patients, Hoffer and Osmond found that schizophrenics treated without niacin or nicotinamide had a gloomy future, over half requiring rehospitalization at least once within five years of their original discharge. Of the niacin and nicotinamide patients, only one sixth needed additional hospital care during the same five year period. Numerous other studies over a twelve year period confirm these findings (Hoffer & Osmond, 1966, pp. 138-140).

Nicotinic acid is preferred over nicotinamide because it reduces the level of cholesterol in the bloodstream. Boyle and others feel that nicotinic acid may therefore be effective in reducing coronaries and arteriosclerosis. Nicotinic acid dilates the blood vessels just beneath the skin, producing a flush effect over the upper half of the body. Some patients find this to be embarrassing or annoying, but, otherwise, no harmful effects result. Hoffer and Osmond refer to their treatment program as Megavitamin B-3 Therapy, so called because massive doses of nicotinic acid (niacin) are the main component (Hoffer, 1967, pp. 11-12).

Hoffer and Osmond group schizophrenics into four types and plan the treatment program accordingly. Type I consists of all outpatients, schizophrenics who are still able to function in

the community and cooperate effectively in their treatment. They are given 3 to 18 grams of nicotinic acid or nicotinamide by mouth daily. Barbiturates, tranquilizers, and antidepressants may also be used if the patient is excessively agitated(25-75 mg. of librium daily in severe cases). 3 grams of ascorbic acid are also given daily throughout their treatment. If the patient responds (as shown by clinical state, subjective account and HOD), the Vitamin B-3 (nicotinic acid) and Vitamin C are continued for at least one year. After one year the medication is discontinued and the patient is observed carefully. If signs of relapse develop, the medication is resumed.

Type II consists of all schizophrenics who do not respond to Type I treatment and all schizophrenics who are admitted to a mental hospital, excluding those who have been hospitalized more than five years. Type II therapy consists of 6 to 10 treatments of electroconvulsive therapy at a rate of 3 per week. In addition, 3 to 18 grams of nicotinic acid or nicotinamide are prescribed daily, and sedatives, tranquilizers, and antidepressants may be used as needed. If HOD scores show a major decrease, the patient is discharged one week after the last ECT. After discharge, Type I medication is continued for one year.

All schizophrenics who do not respond to Type II therapy are classified in Type III. Therapy consists of 3 to 5 ECT treatments per week and 2 grams of penicillamine per day, in

addition to the regular 3 to 18 grams of nicotinic acid daily. Nicotinamide should not be used in Type III cases. The penicillamine is continued for 10 to 20 days unless the patient's temperature elevates to 103° F. or he develops a rash or other allergy. In this case the penicillamine is discontinued. After discharge, Type II therapy is continued.

All schizophrenics who do not respond to Type III therapy are grouped in Type IV. Therapy for Type IV patients is varied, depending on the severity of the schizophrenia. Type IV schizophrenics are those who have lost a large number of neurons due to adrenolutin poisoning. Therefore, recovery at best is usually only partial. Heavy doses of vitamins and tranquilizers are given. High doses of thyroid hormone (3 to 12 grains per day) are given to set the pulse at 100-110. The physician must watch for thyroid tremor. Vitamin B-3 is continued at 12 to 25 grams per day, and valium (muscle relaxant and anticonvulsant) is given for 14 days at 90 mg. per day then at 30 mg. per day or less. The butyrophenones (antipsychotic drugs), haloperidol and trifluperidol, are being used in research, and high doses of antidepressants are also used.

In general, schizophrenics can consume huge quantities of Vitamin C before normal quantities are excreted in their urine. This suggests that it is beneficial for them to receive large doses of ascorbic acid. Vitamin B-1 (thiamine) reduces depression in many schizophrenics. The dose is 1 to 2 grams per day.

Vitamin B-6 (pyridoxine) is essential for the conversion of tryptophan, an amino acid, into nicotinamide adenine dinucleotide (NAD) in the body. Doses of 300 to 500 mg. per day are recommended.

In addition to medication, Hoffer and Osmond recommend supportive and reassuring psychotherapy, a nutritional diet, and education and resocialization if necessary (Hoffer, 1967, pp. 14-16).

The adrenochrome-adrenolutin theory of schizophrenia is only one of several which have been introduced. These are typical of the growing trend toward putting psychiatry on a sounder biochemical basis. Research continues on other vitamins and their effects on mental function. Deficiency of Vitamin B-12, cyanocobalamin, leads to mental illness, often even more pronounced than accompanying physical defects. L (+) - glutamic acid, an amino acid normally present in high concentration in the brain and nerve tissue, has also been studied. In 1944 Price, Waelsch, and Putnam reported favorable results for glutamic acid therapy of convulsive disorders. One out of three or four patients with petit mal epilepsy benefited from the therapy. Zimmerman and Ross then reported an increase in maze-running learning ability of white rats given extra amounts of glutamic acid. Zimmerman and others reported that doses of 10 to 20 grams of glutamic acid per day (given in three doses with meals) improved personality and increased intelligence

by 5 to 20 I.Q. points. These are only selected examples of research covering a broad range of neurochemistry.

Pauling (1968) feels that the brain is more sensitive to changes in concentration of vital substances than are other organs and tissues of the body. This could explain why mental symptoms often appear before a physiological reaction is detectable. Concentration of vital chemicals could measure normal in the blood and yet be deficient in the brain and nervous system. Pauling feels that eventually physicians will be able to measure neurochemical deficiency and prescribe a specific biochemical therapy (Pauling, 1968, pp. 269-271).

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