

Glucose Tolerance in Schizophrenia

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The importance of abnormalities in carbohydrate metabolism in psychiatric disorders has received little attention in spite of the pioneering work of Dr. Seale Harris in the 1920V, who outlined the wide range of symptoms that varying degrees of the hypoglycemic state can produce. The medical community has recognized the seriousness of the insulinoma and the necessity for its treatment, but often has given short shrift to the ideas of functional hypoglycemia and early or pre-diabetes. In recent years, some physicians^{2 3 4} and others have become interested in the effects of altered carbohydrate metabolism in, psychiatric disorders. These investigators have found that a surprisingly large percentage of their patients show abnormalities on the standard five-hour glucose-tolerance test, that treatment with a high-protein low-carbohydrate diet generally brings about improvement, and that the patient's human tendency to violate the diet often results in a relapse in symptomatology which can be remedied by a return to a strictly enforced diet.

The incidence of abnormal carbohydrate metabolism is important in the various psychiatric disorders such as neurosis, alcoholism, learning disorders, manic depressive illness, etc. However, it is the purpose of this paper to examine carbohydrate alterations in schizophrenia.

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For some patients, rapidly shifting blood sugar levels appear to be the main cause of their schizophrenic symptomatology or metabolic misperception (a term proposed by the Committee on Therapy of the American Schizophrenia Association to replace the less descriptive term schizophrenia). The following description illustrates this possibility:

Joseph, aged 13, had been a well-behaved bright boy who got along well with both his peers and adults until approximately one year before I saw him. At that time, he began to lose interest in his schoolwork and progressively became a discipline problem in school. His fine academic performance progressively deteriorated. At times he was withdrawn and at other times irritable and stubborn. Depressed and fearful, he talked about suicide. He was seen in weekly psychotherapy by a psychologist, with periods of improvement and relapse, for six months. For the next three months, he was given increasing doses of niacinamide and ascorbic acid to the level of 9 gm of each, daily. His anxiety lessened; he no longer talked of suicide, but otherwise was little changed, his schoolwork continuing on a failure level.

I evaluated the boy in October, 1968. His Hoffer-Osmond Diagnostic test was in the schizophrenic range with many perceptual distortions and occasional auditory and visual hallucinations. He described inconsistent headaches, blurring and doubling of vision, shakiness, confusion, bad thoughts

spinning around his head beyond his control, and periods of feeling weak. He kept a notebook which was replete with persecutory ideas, misinterpretations and distortions, and descriptions of his agitation. My impression was that of early schizophrenia possibly complicated with hypoglycemia. Triavil was prescribed and a glucose-tolerance test was ordered. Results were as follows: fasting 66; 1 hour, 142; 2 hours, 131; 3 hours, 119; 4 hours, 114; 5 hours, 120; 6 hours, 67. Because of the borderline nature of the results, Joseph was referred to Dr. Ralph Shaw of the Hahnemann Medical College for more thorough evaluation. A five-hour glucose-tolerance test with insulin and fucose levels gave the following figures:

TIME hours	GLUCOSE mg%	FUCOSE mg%	INSULIN uU/ml
fasting	109	43	20
1/2	183	72	35
1	184	46	30
2	164	55	25
3	142	41	35
4	110	37	20
5	137	54	55

Glucose values indicated diabetes mellitus. Fucose values were all elevated. Insulin values were not elevated but fluctuated widely out of proportion to the blood glucose levels.

Dr. Shaw's interpretation was, "It now seems reasonably clear that Joseph had prediabetes with hypoglycemia as late as last spring and that the hypoglycemic spells were contributing to his anxiety. Around September, his pancreas was not able to meet the demands for insulin **and** started into exhaustion atrophy with the development of hyperglycemia. At present, Joseph is frankly diabetic with early dysinsulinism".

Joseph was started on a diabetic diet and DBI 50 mg twice daily. He was followed by Dr. Shaw and Dr. Rittmayer, his psychologist. Three months later his mother phoned me with a delighted report, "My son is back!". Joseph was improving steadily.

In May of 1969, re-evaluation by the school

psychologist indicated improvement in all areas and an increase in his WISC IQ score from 125 to 135. His school report card for the fall trimester of 1969 showed E for excellence in all his subjects, accompanied by glowing reports from his teachers. Joseph had continued asymptomatic with good control of his diabetes when last reported on in the summer of 1971.

Glucose-Tolerance Tests of 500 Schizophrenics

The following are definitions of terms as used in this presentation:

1. Diabetes Mellitus (including early diabetes, pre-diabetes or chemical diabetes). Blood sugar level of 160 mg percent or more at one hour accompanied by blood sugar level of 120 mg percent or more at two hours.
2. Flat curve — less than a 20 mg percent blood sugar rise over fasting level after ingestion of glucose (excluding one half-hour value).
3. Hypoglycemia ... any value falling more than 10 mg percent below the normal fasting range of the test employed.
4. Relative hypoglycemia ... any value 20 mg percent or more lower than the fasting specimen.

The author routinely employs the five-hour glucose-tolerance test, utilizing 100 gm of glucose or its equivalent in all schizophrenic patients.

Five hundred patients were taken in order as they were seen in the office or in the general hospital. Patients were between the ages of 12 and 60 years with a preponderance in the late teens and early twenties. Ninety percent were out-patients. The patients tested in the hospital had been there less than two weeks. The types of diets followed by patients were obviously diverse. Patients were tested without special dietary preparation, the purpose being to test their reaction to glucose in their usual nutritional state, rather

than putting them into an artificial state by giving high-carbohydrate feedings for several days before the test. The results were as follows:

1. Normal 23%.
2. Diabetes 22%.
3. Flat curve 25%.
4. Hypoglycemia 28%.
5. Relative Hypoglycemia 49%.

Many of the patients had a combination of one or more of the abnormalities as, for example, having diabetic values in the first and second hour of the test and experiencing a drop to hypoglycemic levels in the one of the later hours of the test in a pattern of dysinsulinism.

Results in this fairly large sample confirm that carbohydrate metabolic abnormality is a frequent presenting problem in schizophrenia. I know of no large studies of the general population which indicate the incidence of hypoglycemia, relative hypoglycemia, and flat curves. However, the incidence of diabetes (as defined by the glucose-tolerance test figures of 160 mg percent at one hour and 140 mg percent at two hours) in the general population in the United States is put at 2 percent known cases and 1 percent undetected cases. Our sample indicates seven times the general population incidence of diabetes. Our figures parallel the findings of Watzkin at the Veterans' Administration Hospital at Brockton, Massachusetts, where, in addition to 4 percent of known diabetes, 16.4 percent of the remaining 359 men showed a diabetic curve on a two-hour glucose-tolerance test.

Insulin Levels

In an effort to better define and control the more difficult carbohydrate metabolic problems of some of the patients, 40 were studied with glucose, insulin, and fucose blood determinations during five-hour glucose-tolerance tests. Several of the first

patients showed very high insulin and fucose levels out of proportion to the glucose abnormalities. However, the apparent uniqueness of the pattern soon became diluted with other patients in the schizophrenic sample, and the group as a whole could not be distinguished from other groups of diabetics and hypoglycemics on the basis of the insulin, fucose, and glucose levels.

Glucose Tolerance of Other Psychiatric Patients

Three hundred and eighty-one psychiatric patients with a variety of diagnoses other than schizophrenia underwent five-hour glucose-tolerance tests under the same conditions as the schizophrenic group. The results were as follows:

Normal 17% Diabetic 25% Flat 23%

Hypoglycemic 22% Relative hypoglycemia 63%

Comparison of the schizophrenic and non-schizophrenic group indicates that carbohydrate metabolic abnormalities are by no means limited to the schizophrenic group.

Summary

Carbohydrate metabolic abnormality as determined by a standard five-hour glucose-tolerance test was found in 77 percent of a sample of 500 schizophrenic patients and in 83 percent of a sample of 381 psychiatric patients with diagnoses other than schizophrenia. The insulin, fucose, and glucose values on five-hour glucose-tolerance tests of a group of 40 schizophrenic patients could not be differentiated from values of other groups of diabetics and hypoglycemics who did not carry a psychiatric diagnosis.

One example was cited in which schizophrenic symptomatology appeared to

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be based almost wholly on alterations in blood sugar and in which control of blood sugar eliminated the schizophrenic syndrome. This case was chosen as a dramatic illustration of this phenomenon. In the author's experience, cases of this sort are rare. The usual experience with vigorous treatment of carbohydrate metabolic abnormality in the schizophrenic is an enhancement of the improvement being brought about by concurrent other methods of treatment. It is my opinion that carbohydrate metabolic abnormality can be listed, as are pernicious anemia and hypothyroidism, as the cause of a small percentage of schizophrenia, but that usually it is present as a complicating factor rather than as the main etiological agent. The primitive state of our knowledge in regards to the biochemistry of schizophrenia, diabetes, and hypoglycemia provides no basis for an explanation of the high incidence of carbohydrate metabolic derangements in psychiatric illness in general, and schizophrenia in particular.

References

1. HARRIS, S.: Hyperinsulinism and Dysinsulinism. JAMA 83:729-733, 1924.
2. COTT, A.: Treatment of Ambulant Schizophrenics with Vitamin B-3 and Relative Hypoglycemic Diet.). Schizophrenia 1:189-196, 1967.
3. MEIERS, R. L.: Relative Hypoglycemia in Schizophrenia. J. Schizophrenia 1:204-208, 1967.
4. SALZER, H.: Relative Hypoglycemia as a Cause of Neuropsychiatric Illness. Journal National Medical Assn. 58:12-17, 1966