

# Relapsed Schizophrenics: Earlier Discharge from the Hospital After Cereal-Free, Milk-Free Diet

BY F.C. DOHAN, M.D., AND J.C. GRASBERGER, M.D.

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*Routinely treated schizophrenics, who on admission were randomly assigned to a diet free of cereal grains and milk while on the locked ward, were discharged from the hospital about twice as rapidly as control patients assigned to a high-cereal diet. Wheat gluten secretly added to the cereal-free diet abolished this effect. These and previous findings suggest that cereal grains may be pathogenic for those hereditarily predisposed to schizophrenia just as they are for celiac disease, a disorder that may be genetically related.*

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WE HAVE PREVIOUSLY REPORTED that a cereal-free, milk-free diet hastened the improvement of relapsed schizophrenics ( $p < .01$ ) as judged by the duration of their stay on a locked ward (1, 2). This was apparently not due to psychological factors affecting staff or patients, since the effect disappeared when wheat gluten was secretly added to the diet. This suggests that diet is of therapeutic value and that cereal grains may be one of the pathogenic factors affecting those susceptible through heredity to schizophrenia. This hypothesis (3) is further supported by the following:

1. Epidemiologic data demonstrating a strong correlation ( $r = 0.96$ ,  $p < .01$ ) between first admissions for schizophrenia and the consumption of wheat plus rye (2, 3).
2. Observations indicating that celiac disease (gluten enteropathy), which is probably based on polygenic inheritance (4) and is ameliorated by not eating wheat gluten and its analogues in other cereal grains, and schizophrenia, which is probably also polygenic (5), occur in the same individual more frequently than would be expected by chance (2, 6).
3. Data from sizable samples of schizophrenics in the pre-phenothiazine era provided findings similar to those in celiac patients, including gastrointestinal and other symptoms (7-10), metabolic changes (9, 11), failure to

gain weight on high-calorie diets (11, 12), and histologic changes in the intestines and mesenteric lymph nodes (10, 13, 14).

4. Reports of frequent psychiatric disturbances in celiac patients, including one instance of hallucination (15, 16), which may rapidly be made manifest by gluten administration (6), show improvement soon after the removal of gluten from the diet (16-18), and in some cases are similar to disturbances seen in schizophrenia (6, 15).

The purpose of our present study was to examine the effect of a cereal grain-free, milk-free diet upon relapsed schizophrenics as measured by another and more commonly used index of improvement than the length of stay on the locked ward, which was the index used in our previous study (1, 2). We now report data that have become available since that time—the length of stay until discharge from the hospital of relapsed schizophrenics who were on the test diets during their stay on the locked ward. We included only those patients readmitted or admitted for the first time to the Coatesville, Pa., Veterans Administration Hospital during our previous study periods (I and II) and during an additional admission period (IIIa). Our previous study included patients transferred to the locked ward from the open wards as well as those assigned to the locked ward on admission to the hospital.

## METHOD

All subjects were male veterans. The means and distributions of their ages by experimental groups did not differ significantly. The mean for all subjects was 38 years. The diagnostic criteria were those outlined in the 1952 edition of the American Psychiatric Association's *Diagnostic and Statistical Manual*. Aside from the diet while on the locked ward, all patients were treated routinely during their period on the locked ward and after their release to the open wards. Chlorpromazine and thioridazine were the most frequently administered antischizophrenic medications. After review of their cases at a staff conference, patients who were improved sufficiently or considered likely to experience no further benefit from hospitalization were discharged.

We report here the length of time from admission to discharge from the hospital (within approximately one year after the end of each admission period) for those schizophrenics who entered the locked study ward on the day of their admission to the Coatesville Veterans Administration Hospital as new admissions or as read-

Dr. Dohan is Associate Professor, William Pepper Laboratory of Clinical Medicine, Hospital of the University of Pennsylvania, and Medical Research Scientist, Eastern Pennsylvania Psychiatric Institute, Philadelphia, Pa. 19129. Dr. Grasberger is Assistant Chief of Staff (Psychiatry), Veterans Administration Hospital, Coatesville, Pa.

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TABLE 1

*The Effect on Discharge from the Hospital of a Diet Free of All Cereal Grains and Milk (CFMF) Compared with High-Cereal Diet (HC)*

Day After Admission	CFMF Diet (N = 59)		HC Diet (N = 56)		Probability Difference Was Due to Chance* (Percent)
	Cumulative Number Discharged	Cumulative Percent	Cumulative Number Discharged	Cumulative Percent	
30	6	10.2	2	3.6	15.3
60	17	28.8	7	12.5	2.6
90	22	37.2	9	16.1	0.9
120	24	40.7	12	21.4	2.1
150	26	44.1	12	21.4	0.8
180	27	45.8	15	26.8	2.7
360	30	50.8	22	39.3	14.5

\*Fisher's exact method.

missions to it. Only those who remained on the locked ward longer than one day are included in the analysis.

During the three admission periods, all patients who entered the locked ward from either outside or inside the hospital were immediately randomly assigned (initially by odd or even Social Security numbers and later by random numbers in balanced groups of four) to various experimental diets. The experimental diets were provided only during the patients' stay on the locked ward. After release from the locked ward to an open ward (which usually occurred by the 15th day), all patients were subjected to the same diet, i.e., the usual hospital diet. This diet afforded ample opportunity to consume large amounts of cereal grain products and milk.

During period I (175 days) and period IIIa (148 days) patients were randomly assigned either to a diet free of all cereal grain and milk products (CFMF diet) or to the usual milk-containing hospital diet, which was made somewhat higher in cereal grains (e.g., spaghetti instead of potatoes)—the high-cereal diet (HC diet). Milk was omitted from the CFMF diet because it produces a relapse in some celiac patients and thus, we hypothesized, may be harmful to some schizophrenics. During admission period II (143 days) patients were randomly assigned to either the HC diet or to the CFMF diet to which wheat gluten (about 19 gm./day) had been secretly added. This is approximately the amount consumed in breads, cakes, and so forth by the subjects on the HC diet. Strict mealtime and between-meal diet discipline was attempted for all patients during their stay on the locked ward throughout the entire study.

At the end of each admission period the patients were continued on the locked ward diets for a week to ten days, thus providing a "corridor" before the beginning of a new period. Patients admitted during the corridor period were not included in the experiment. Only 11 of the patients in this study were not released from the locked ward to an open ward before the beginning of a new period. All of them had been on either the HC or CFMF plus gluten diet. This is in accord with our previous observation that a CFMF diet is associated with an earlier re-

lease from the locked ward. Patients transferred to the medical or surgical wards or to another hospital were not included in this study.

Those schizophrenics who were admitted to the hospital as new admissions or readmissions during each of the admission periods and who were assigned to a particular experimental diet can be considered one cohort. Since we hypothesized that the CFMF diet would be associated with earlier discharge from the hospital and this diet was given during periods I and IIIa, the results from the two cohorts that were assigned to the CFMF diet in these two periods were combined for analysis, as were the results from the two HC cohorts.

## RESULTS

Table 1 demonstrates that the proportion of relapsed schizophrenics in the CFMF diet group who were discharged from the hospital during the first six months was considerably and significantly greater than that in the HC group. In contrast, table 2 shows that when gluten was secretly added to the CFMF diet this difference did not occur.

### *CFMF Diet Versus HC Diet*

The significance of the differences in the cumulative proportions of the 59 CFMF schizophrenics and the 56 HC schizophrenics discharged from the hospital at successive ten-day intervals after admission was analyzed by Fisher's exact method. Table 1 shows the results at 30-day intervals. The cumulative percentage discharged of the CFMF group at the end of each ten-day interval from day 40 through day 190 was significantly greater than that of the HC group. The probability that the differences between the two groups was due to chance alone was less than three percent in 13 of the 16 comparisons. On days 90, 150, and 160 the probability was less than one percent. Thus, it seems unlikely that the more rapid discharge of the CFMF group was due to chance alone.

The increased rate of discharge occurred during the

TABLE 2

*The Effect on Discharge from the Hospital of Adding Wheat Gluten to the Diet Free of All Cereal Grains and Milk (CFMF) Compared with High-Cereal Diet (HC)*

Day After Admission	CFMF + Gluten Diet (N = 17)		HC Diet (N = 25)		Probability Difference Was Due to Chance* (Percent)
	Cumulative Number Discharged	Cumulative Percent	Cumulative Number Discharged	Cumulative Percent	
30	0	—	1	4.0	59.5
60	2	11.8	2	8.0	53.8
90	4	23.5	3	12.0	28.4
120	4	23.5	5	20.0	53.7
150	5	29.4	6	24.0	48.2
180	6	35.3	7	28.0	43.3
360	6	35.3	8	32.0	54.1

\*Fisher's exact method.

first 90 days after admission. The cumulative proportion discharged at the end of 90 days after admission was 37.2 percent for the CFMF group, compared with 16.1 percent for the HC group. Furthermore, of the number in each diet group who were in the hospital on days 0, 30, and 60, the proportion discharged in the following 30 days was 10.2, 20.8, and 11.9 percent for the CFMF group and 3.6, 9.3, and 4.1 percent for the HC group; that is, the absolute discharge rate of the CFMF group for each of the three 30-day intervals was more than twice that of the HC group. However, after that time the percentage of the remainder discharged was about the same for both groups.

Considering only those patients discharged from the hospital, the median day of discharge for both groups combined was day 65; the median day (interpolated) was day 102 for the HC group and day 53 for the CFMF group. The average time until discharge for the discharged CFMF patients (77 days) was 55 percent of that of the discharged HC patients (139 days).

Only one patient was admitted to the hospital twice, each time on a different diet. When randomly assigned to the HC diet he remained on the locked ward for 17 days and left the hospital without permission (AWOL) on day 65. When he was readmitted 11 months later and randomly assigned to the CFMF diet he stayed seven days on the locked ward and was discharged on day 22.

Of the 22 HC patients who were later discharged, 10 were returned to the locked ward one to six times because of their behavior on the open ward. Of these, three were then randomly assigned to the CFMF diet. They were discharged 21, 78, and 87 days later, all in less than the median time to discharge (102 days) for the HC group. Of the 30 discharged schizophrenics in the CFMF group, only three reentered the locked ward (one or two times), all on the CFMF diet.

#### *CFMF Plus Gluten Diet Versus HC Diet*

Analysis by Fisher's exact method at ten-day intervals of the cumulative proportions discharged from the CFMF plus gluten diet versus the HC group showed

that the lowest probability that the differences were due to chance alone was 28.4 percent and that all other values except one were greater than 40 percent. Thus, as is shown in table 2, there was no significant difference in the rate of discharge between the HC group and the CFMF group when gluten was secretly added to the CFMF diet.

#### DISCUSSION

During the first 90 days after admission to the hospital, those schizophrenics assigned to the CFMF diet were discharged more than twice as fast as those in the HC control group. After that period the rates became similar. We suggest this might be because the subjects were on the CFMF diet only during the time they were on the locked ward (prior to their release to an open ward), which for 76 percent of the entire CFMF group was no more than 15 days. Thus, any therapeutic effect of this brief period on the CFMF diet may have lasted for only a few months after resumption of the normal hospital diet. It is also possible that only a proportion of those diagnosed as schizophrenic respond to a CFMF diet.

We have previously observed (1, 2) that the effect of the CFMF diet on improvement of relapsed schizophrenics was most prominent within the first week or two. The effect on the discharge rate occurred in the first three months. Perhaps a longer period on the CFMF diet would have extended this effect. The psychological symptoms of celiac (gluten enteropathy) patients also usually improve considerably within a week or two, often within a few days (16-18), when they are placed on a "gluten-free" diet (i.e., omitting foods made from wheat, rye, barley, and sometimes oats). The symptoms often but not always recur in weeks to years after resuming the usual gluten-containing diet. However, we are unaware of reports of sustained improvement of celiac patients after a period as short as the two to ten days of this diet experienced by 24 (80 percent) of the 30 discharged CFMF schizophrenics.

Many observers state that celiac patients, after being

on a gluten-free diet, find they can eat gluten-containing food for weeks to years with no (or only minor) subjective symptoms prior to clinical relapse. Unfortunately, the length of time from starting a gluten-free diet to the development of tolerance to gluten and its analogues has not been well studied. Cooke and his co-workers (19) in a report on 50 celiac patients noted that 25 of them were eating foods containing gluten, seven of them without any treatment whatsoever after the initial treatment period. They noted, as have others, that after the initial treatment, apart from the intestinal biopsy findings of mucosal atrophy, there was surprisingly little difference between celiac patients who were on a gluten-free diet and those who were not. It is customary, nevertheless, to recommend that the gluten-free diet be maintained for many years. The clinical reports that "psychic stress" often precedes relapse and the careful observation of Grant that relapses in celiac patients tolerating gluten occurred when the life situation was such that the patient "gave up" (20) are of considerable interest in view of the probable role of psychic factors in the relapse of schizophrenics.

In contrast to the beneficial effects of the CFMF diet, the relapsed schizophrenics on the CFMF diet to which wheat gluten was added (without the knowledge of staff or patients) were not discharged from the hospital significantly faster than their temporal controls on the HC diet. This finding suggests that the effect of the CFMF diet on the discharge rate was not due to any bias of the patients or staff. During this period there was also no difference in the rate of release from the locked ward of the HC and CFMF plus gluten groups composed of schizophrenics entering the locked ward from open wards or as new admissions to the hospital (1, 2).

These adverse effects on relapsed schizophrenics of gluten added to the CFMF diet indicate that, as in celiac disease, "toxicity" is associated with the gluten fraction of wheat. However, epidemiologic data indicate that schizophrenia occurs, although possibly with lesser frequency, in societies that eat no wheat or rye but do eat other cereal grains (3) such as maize and millets, which contain gluten-like proteins but with a lesser proportion of glutamic acid, glutamine, and proline.

## CONCLUSIONS

We believe that the beneficial effect of the cereal grain-free, milk-free diet on discharge rates adds strong support to the hypothesis that cereal grains may be involved in the pathogenesis of schizophrenia (1-3, 6, 15) as well as in celiac disease. We therefore suggest that the effects of this diet on acute new or recently relapsed schizophrenics deserve careful testing by other investigators. If the effect of diet on persistently chronic schizophrenics is to be tested we suggest the diet be continued for at least six months to a year. The examination of unmedicated active schizophrenics, who have been on a high gluten-containing diet for weeks or months, by the same techniques used in studying celiac disease (in particular, per-

oral intestinal biopsy) should be fruitful, as should an investigation of the possibility that one or more genes may be common to the two diseases.

The annual direct plus indirect cost of schizophrenia in the United States for the two to three million Americans carrying this diagnosis was recently estimated as approximately 14 billion dollars (21). If diet proves to be an effective long-term therapeutic adjunct, as our preliminary short-term experiments and epidemiologic observations lead us to postulate, the tremendous human burden and financial costs of this relatively common disorder should be substantially decreased.

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