

# Diagnosis and Treatment of Celiac Disease

## REPORT OF 603 CASES

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WE present in this paper the results of our experience with 603 cases of celiac disease from which has emerged a useful method of diagnosis of this confusing condition and, more important, an effective cure by diet which we have found successful in cases of all types and degrees of severity.

Since the etiology of celiac disease is unknown and its symptoms occur in many other conditions, it may be helpful to review briefly the history of attempts to find a cure, especially by dietary methods, and to describe the clinical picture of the disease. We shall then outline our diet in detail, report statistically on our 603 cases, and suggest further lines of study.

### HISTORY

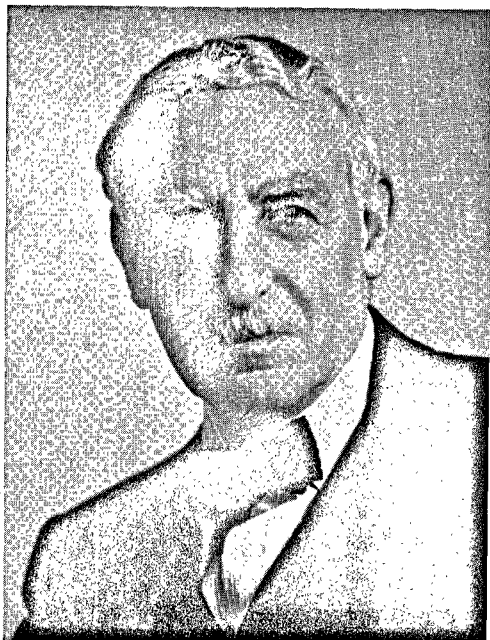
At the turn of the century, celiac disease was almost unknown in this country. American medical literature published no articles on the condition; the general practitioner knew nothing of it, the pediatrician little more. He had perhaps read Gee's report "On The Coeliac Affection,"<sup>1</sup> published in 1888, describing the extreme emaciation, huge abdomen, failure of growth with resulting infantilism, and characteristic large, pale, fatty stools—all symptoms of advanced cases often ending in death. From Gee he gained no picture of mild or incipient cases, nor any concept of the true nature of the disease, beyond the conclusion that treatment must depend upon diet. Gee's tentative dietary suggestions proved ineffective and, later, thoroughly unsound.

A year after Gee's report, R. A. Gibbons wrote

an article in the *Edinburgh Medical Journal*<sup>2</sup> which received little attention then or later. His suggestion that celiac disease involved a functional derangement of the nervous mechanism controlling the digestive glands warrants more attention and investigation than it has ever received.

In 1901-1902 Bramwell<sup>3</sup> reported on his treatment of a case of infantilism by means of pancreatic extract. In 1903, W. B. Cheadle<sup>4</sup> attributed the pale color of stools in celiac disease to absence of bile in the feces and blamed the biliary mechanism for the condition. In 1909, Heubner<sup>5</sup> described the severe intestinal insufficiency in children past infancy resulting in retardation of growth. Heubner noted that protein digestion was not interfered with but that the ingestion of fats and carbohydrates caused increase in symptoms.

Meanwhile, in the United States, Dr. L. Emmett Holt had turned his attention to celiac disease and awakened the interest of a colleague, Dr. Christian Herter, then Professor of Therapeutics and Pharmacology at Columbia, who went deeply into the laboratory phases of the subject and, with Dr. Holt's assistance, into the clinical phases as well. Herter's conclusions appeared in 1908 in his book "On Infantilism From Chronic Intestinal Infection,"<sup>6</sup> suggesting that the disturbance resulted from the bacterial action of *B. bifidus* and *B. infantilis*. The importance of bacteria in this condition never received complete support. Some of Herter's observations, namely, that proteins were very well borne in celiac disease, fats moderately well borne, and that carbohydrates were very badly



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tolerated, indicated the most rewarding path to follow, although his concern with the role of bacteria prevented his seeing the significance of this.

Two young assistants of Dr. Holt at the Vanderbilt Clinic whom he had interested in celiac disease were Dr. John Howland and Dr. Sidney V. Haas. Each independently followed up Herter's observations. In 1921, Dr. Howland, in his presidential address before the American Pediatric Society, read a paper on "Prolonged Intolerance To Carbohydrates."<sup>7</sup>

Although Howland did not refer specifically to celiac disease, he described two conditions, temporary and prolonged intolerance to carbohydrates. The latter are cases of celiac disease, described as clearly and accurately as in any literature on the subject. He found that of all the elements of food, "carbohydrate is the one which must be excluded rigorously; that with this greatly reduced the other elements are almost always well digested, even though the absorption of fat may not be so satisfactory as in health." Howland's treatment was a high-protein diet based on protein milk, and it achieved greater success than any previously set

forth. But at the point when carbohydrates were added to the diet, he encountered frequent recurrence of symptoms.

IN November, 1923, before the Section on Pediatrics of the New York Academy of Medicine, Sidney V. Haas read a paper on "The Value Of Banana In The Treatment Of Celiac Disease,"<sup>8</sup> presenting 8 patients who had been cured by a high protein diet, plus banana and other fruits and some vegetables which supplied carbohydrates in a form that was well borne even by advanced cases of celiac disease.

Five years later, in 1928, Fanconi<sup>9</sup> of Zurich published a paper reporting 45 cases of celiac disease, in which he substantiated the Haas thesis as to the value of fruits and vegetables in this disease. However, he used buttermilk or dry skimmed milk, which we have always found unsatisfactory. Fanconi observed that cane sugar and grain foods, even in small quantities, were decidedly unfavorable in their effects, but advised after the first few weeks of treatment a careful allowance of bread crust and zweiback for the dubious reason "that the child should not entirely forget how to chew."

In 1929, Hess-Thaysen<sup>10</sup> published his important monograph on nontropical sprue. In this he pointed out the possibility that celiac disease was identical with sprue, and stressed the occurrence of steatorrhea in these diseases, which he called idiopathic steatorrhea.

Leonard Parsons, Professor of Pediatrics at the University of Birmingham, England, delivered the first Rachford Memorial Lecture in this country in 1932,<sup>11</sup> presenting a thesis that has caused confusion in the treatment of celiac disease even to the present day. Parsons' high standing in the profession gave great weight to his statement that fats were at fault in celiac disease. As a result, the opinion is still widely held that fat must be excluded from the diet or reduced to a minimum. It should be noted, in this regard, that rickets was prevalent among Parsons' cases.

In 1938, Dr. Dorothy Andersen<sup>12</sup> described the condition of cystic fibrosis of the pancreas, which presents many points of similarity to the clinical picture of celiac disease. Thinking that steatorrhea, commonly found in both conditions, was caused by fats in the diet, she advocated a high protein, high carbohydrate, low fat diet. In 1947,<sup>13</sup> however, she presented evidence

to show that steatorrhea was not a basic condition in celiac disease.

Many of the standard works on pediatrics<sup>14, 15</sup> today state that sugar or starch feeding will increase diarrhea but advocate banana, whose carbohydrates are well tolerated, as a basic part of the diet. However, they usually prescribe low fats, at the same time.

This brief summary mentions only the chief points in the history of the dietary approach to celiac disease. Much excellent laboratory work on the chemistry and pathology of the condition has been reported, especially in the past twenty years, but its history does not belong in this clinical report on treatment by diet. The increase in interest in celiac disease is evidenced by the bibliography on the subject. A review of the literature shows that in the thirty-five years between Gee's report in 1888 and the first paper on the value of the banana in 1923, there were 99 papers published. In the twenty-five years since that time, 405 papers were published. Up to 1923 there were only 31 American papers, while 112 have been printed since that date.

In this literature, even the more modern, there has been great confusion not only as to diagnosis and treatment of the disease but as to its nature and name. At one time or another it has been considered a bacterial infection, a disturbance of the nervous system, identical with sprue, an allergy, avitaminosis, fat intolerance, carbohydrate intolerance, hypothyroidism, and constitutional weakness. Some writers have doubted that it actually is a disease.

We speak of celiac disease deliberately as a disease because it is a condition of abnormal physiology with a characteristic syndrome, the symptoms of which respond favorably to a definite mode of therapy.

Recently some investigators have attempted to break down the symptom complex into various types. The present state of understanding of celiac disease resembles that of typhoid fever sixty or seventy years ago. Then there was typho-malaria, typho-pneumonia, typho-meningitis, the abortive form, the afebrile form, the ambulatory form, and even typho-lumbricosis, a tribute to the intestinal parasite of that name. With the discovery of the Eberth bacillus and later the Widal reaction, all this was changed. All these conditions became typhoid fever, with varying symptoms. The same clarifying action will occur when the cause of celiac disease is discovered. Meanwhile, attempts to divide and



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subdivide serve only to add confusion to a picture already confused.

#### DEFINITION

**C**ELIAC disease is altered intestinal function signaled by the occurrence of abnormal stools, which are more frequent than usual and altered in physical characteristics. From this altered intestinal function may come varying degrees of disturbance of nutrition, depending upon the duration and severity of the condition and upon the diet. The condition may be protracted or intermittent, and it occurs independently of other known etiologic factors such as specific infections, parasitic infestations, or abnormal anatomy.

Once this altered intestinal function exists, it will continue as long as the ingestion of carbohydrates, other than those found in fruits and to a lesser extent in vegetables, continues. A diet free of all carbohydrates except those in fruits and vegetables results in the disappearance of symptoms, which will recur when forbidden carbohydrates are again ingested. If, however, the exclusion of carbohydrates other than those

in fruits and vegetables continues for a sufficient time, there will be no recurrence of stool abnormalities or nutritional disturbance when forbidden carbohydrates are added.

#### THE CLINICAL PICTURE

With this abstract definition as a framework, the clinical picture of celiac disease may be filled in clearly as to symptomatology, diagnosis, and treatment.

The most important, as well as the most characteristic symptom of celiac disease is diarrhea, which may exist from birth or may begin at any time thereafter, usually within the first few years of life. The stool may be watery, but is usually only soft and mushy, more voluminous than in health, with frequency of from one to ten daily. It is sometimes oily, often mucoid, and usually foul. The color varies from pale cream to greenish yellow. Each attack of diarrhea may last a few days, weeks, or months, but there are intervals when stools return to normal. The recurrence of diarrhea with such intervals of almost normal stools is very characteristic and one of the most valuable diagnostic features available at the present time. In rare cases there is constipation, making diagnosis difficult.

The second most common symptom is irritability and obvious unhappiness, evidenced by whining and crying, coupled with weakness and asthenia and usually anorexia, although in a few cases the appetite is good. These symptoms are the first to disappear with correct treatment, usually clearing up within a week or two.

Next in frequency among symptoms is the failure to gain weight and to grow. In more severe cases there is actual loss of weight. The extreme emaciation so prominently mentioned in classical descriptions of celiac disease occurs only in the most severe cases. Similarly, the large abdomen of the classical picture is found only in advanced cases. It varies in size from day to day and, representing a real anatomic change, outlasts all other symptoms; in fact, even after the disease has been cured, the patient must practically grow up to his abdomen, which, however, finally becomes flat.

Among the common symptoms of celiac disease are abdominal pain and vomiting. Colic is more frequently encountered than vomiting, but both are commonly found up to the time when correct treatment is begun, after which they soon disappear.

Other symptoms that may be mentioned here are definitely subsidiary, and depend upon the malnutrition and the extent of deprivation of specific dietary factors. Some of these are anemia, edema, hydrolability, enlarged heart, photophobia, rachitic manifestations of varying degrees, hemorrhagic states, and pareses.

It is not surprising that celiac disease so often fails to be recognized in its early stages when its primary symptoms are as general and unspecific as diarrhea, irritability, failure to gain, abdominal pain, and vomiting. Moreover, the disease usually begins insidiously, sometimes as a sequel to acute gastrointestinal disturbance or an infection. The bowel disturbance may begin so gradually that it is not taken seriously for some time and is treated only as the result of an unsuitable formula, although changes in formula have no beneficial effect.

The incidence of celiac disease is difficult to estimate. Pediatricians known to be interested see many more cases than others, and if calculations were based upon the number of cases they encounter in relation to their total practice, a false conception of its frequency would result. On the other hand, the average physician sees so few celiac patients that many may pass him unrecognized. Since beneficial results are often not obtained quickly, the patient is taken from one physician to another, thus increasing the difficulty of estimating the incidence of the disease. We do know, however, that it is much more common than was formerly thought. It spares no group; the wealthy, the poor, the well-fed, the starving are equally subject to it.

CELIAc disease may occur at any age, although it is encountered most commonly among children under 6 years of age. There is evidence which warrants the suggestion that in adults the condition is identical with nontropical sprue. Many investigators have stated flatly that celiac disease never occurs in breast-fed infants, but our records and the literature show many such cases. Another common assumption is that the condition never occurs under 1 year of age; in Sidney Haas' first paper on celiac disease in 1923, this statement was made. Subsequent experience conclusively proved the error of this belief. Celiac disease may exist from birth, and it is not at all uncommon under 1 year of age.

Some evidence supports the view that there is a familial tendency toward the disease,<sup>16</sup> as it

has been found in several generations of the same family, in twins, in brothers and sisters, in cousins, and more distant relatives. But more than one case is infrequently found in the same family at the same time.

#### PATHOLOGY

Although promising laboratory work has been done on celiac disease, the problem must remain a clinical one for the present, owing to the absence of a known etiology. All pathologic abnormalities found in celiac disease are encountered also in other conditions. Some investigators believe that a disturbed pancreatic function is significant, but analysis of duodenal secretions does not contribute essential information.

Examination of the stools is only of supplementary aid. The presence of excess fats is usual, but it occurs also in other conditions, and varies in the same case from one examination to another. Likewise the low blood-sugar curve customarily found in celiac disease is present in other conditions. Hess-Thaysen<sup>17</sup> found it to be present as an inconstant phenomenon in about 5 per cent of normal individuals. Although pathology is found in the pancreas, the liver, and the intestinal wall, and although the autonomic nervous system seems to be implicated, no laboratory procedures have yet succeeded in revealing pathologic conditions that make definite diagnosis possible. The roentgenographic examination shows a moulage pattern but this is also seen in normal children and in deficiency states. The diagnosis of the disease must depend upon clinical symptoms, history, and the effect of the strict celiac diet to be described.

#### DIAGNOSIS

The severe case is relatively easy to diagnose. There can be little doubt that celiac disease is present in a miserable, crying, emaciated child with distended abdomen, flat buttocks, who is unable to stand or sometimes even to sit; a stunted child presenting all the symptoms of avitaminosis, edema, and anemia; a child with a long history of months or years of gastrointestinal disturbance, resulting in frequent stools that are large, pale, oily, and foul. In such cases the picture is clear.

Earlier and milder cases are not so easily recognized, and here the history is of utmost importance. A history of anorexia, prolonged,

intermittent, recurrent diarrhea, with intervals of weeks or months during which the child does fairly well despite an overall failure to gain weight or grow normally—such a history should suggest at once the possibility of celiac disease. It is necessary, of course, to make sure that there are no intestinal parasites and to exclude dysentery and dysentery organisms, as well as amebae and tuberculous peritonitis, gastrointestinal anomalies or obstructions.

The only definite method of diagnosis consists of the response to the correct celiac diet, better termed specific carbohydrate diet, described later in this article. If immediate beneficial results follow the institution of the diet, the case may well be considered celiac disease. If forbidden carbohydrates are then introduced into the diet of such a patient who is doing well, and an attack of loose stools results, this is practically pathognomonic, especially if re-institution of the specific carbohydrate diet controls the diarrhea.

This method of diagnosis was used in the 603 cases analyzed here, and the 370 cases seen over a long period received a treatment, the cornerstone of which was the specific carbohydrate diet. Before examining the cases, therefore, it seems advisable to outline this diet and supplementary treatment.

#### TREATMENT WITH CELIAC DIET

No term has suffered more abuse and misunderstanding than "celiac diet." Literature on the subject reveals many statements that "a celiac diet was used without good result," when actually the diet was no proper celiac diet at all.

One basic principle of the diet must be established firmly and reiterated persistently: *No food may be ingested by the celiac patient that contains an appreciable amount of carbohydrate other than that found in fruits and to a lesser extent in vegetables, and in protein milk.* While this principle may be easily understood, it is difficult in practice always to recognize the existence of the carbohydrates in various foods. Carbohydrates other than those designated often creep into the diet in small quantities unless the strictest attention is paid to every item of food.

THE basis of the specific carbohydrate diet is ripe banana and protein milk. Protein milk should be prepared in one of the three ways

described in the footnote below;\* when the child will not drink protein milk, calcium caseinate milk\* may be used.

Although all fruits may be used later, banana is the most satisfactory and the only safe fruit to be used at the outset of treatment. Its particular value in celiac disease comes from the fact that it is a 20 per cent carbohydrate and thus replaces better than any other fruit the excluded carbohydrates such as cereal, sugars, and potatoes. It has a very low fiber content, is easily obtainable, palatable, and well liked by most children. It may be served raw or baked. Only fully ripe bananas should be given, with no trace of green at the tips, the skin well speckled with brown, and the edible portion soft enough to mash easily. In the unripe banana most of the carbohydrate is in the form of starch which is converted, in the process of ripening, to sugars which the celiac patient tolerates well.

If ripe bananas are not available or practical to use, banana powder may be substituted as the exact equivalent of fully ripe bananas. Another acceptable substitute is dried banana flakes, although these do not invariably give quite as satisfactory results as fresh ripe bananas.

Because various other fruits have qualities which tend to make them laxative, they must be employed judiciously when diarrhea is still active. There need be no curtailment of the amount of banana given. Most canned fruits are forbidden because of added sugar. If cooked

fruits are desired, they may be prepared with saccharin by the family, but the initial product must be known.

The specific carbohydrate diet, in addition to protein milk and fruits, may contain proteins in any form and fats in moderate quantities. Thus meat, fish, and fowl of any kind may be used, and it is not necessary or even advisable to have all the fat removed. All cheese is satisfactory, unless it has been processed by the addition of ingredients to alter the composition; the diet may include any cheese in its initial form, Swiss, cheddar, American, and of course pot cheese.

Gelatine is given for dessert in this diet, but not Jello or other prepared gelatine desserts which contain sugar. Desserts made from pure gelatine, fruit juice, and saccharin for sweetening are well tolerated; honey, dates, and raisins may be used as confections, but some dates are packed in sugar syrup to make them adhere in one mass, and these should not be used.

When brisk diarrhea is controlled, egg is added to the diet. And when the stools are formed and occur no more than two or three times daily, vegetables are given. But they must be added to the diet cautiously, one at a time with a sufficient period between each new introduction to determine their effect. In some cases diarrhea recurs when vegetables are ingested, in which case their use must be postponed. In general, lettuce, tomato, string beans, squash, and carrots are well tolerated. Canned vegetables are not used because many have sugar added. Potato may not be used.

Fats in association with meats in the normal amounts, in the form of butter, and that existing in protein milk are well borne.<sup>16</sup> Sour cream is usually tolerated. The only restriction on fats may come at the beginning of the diet, but when a full and well-rounded diet has been established there need be no restrictions of fat beyond that usually exercised in the diet of healthy children.

\*Protein milk prepared according to Finkelstein and Meyer:<sup>15</sup> One quart milk, warmed to temperature of 98° F. To this is added 1 tablespoon of essence of pepsin. Allow to drain through cheesecloth for one-half hour to separate the whey from the curd. The curd mixed with 1 pint of water, is then rubbed through a fine wire strainer several times, and to it 1 pint of buttermilk is added. The whey which contains most of the sugar is discarded.

Protein milk as prepared by Mueller and Kran:<sup>19</sup> Mix 1 quart of buttermilk (commercial) and 1 quart of water and heat to a temperature of 135° F. Remove from the stove and let stand for one-half hour. The curd by this time is well separated from the whey, 36 oz. of which should be dipped off. The remaining curd and whey are mashed through a fine sieve, and 4 oz. of 20 per cent cream or 4 oz. from top of bottle of milk, and enough water added to bring the mixture to 32 oz.

Powdered protein milk: 12 tablespoons of the powder to 32 ounces of water.

Calcium caseinate milk: Use 4 to 6 tablespoons of calcium caseinate (Mead Johnson's Casec) to 1 pint of water and 1 pint of milk. Mix the Casec with a little cold water (enough to form a smooth paste), pour in the remainder of the cold water. Then pour in the milk and bring the whole mixture to a boil while stirring constantly, then boil actively for one minute. Remove from fire. Let cool. If necessary to sweeten, use one or two tablets of saccharin (1 gr.).

WITH the inclusion of the foods mentioned, the specific carbohydrate diet is complete. Since it is full and well-balanced, it is continued for at least one year, supplemented by certain vitamins. Vitamins A and D should be administered, but cod liver oil is usually not well tolerated. Some of the newer preparations of aqueous soluble A and D are excellent substitutes. One of the preparations of B complex, including folic acid, seems to be desirable. Since anemia is a

regular feature of celiac disease, iron in some form is called for.

IN prescribing this diet, it is almost more important to stress what is *not* fed than what is fed. Any cereal grain is strictly and absolutely forbidden, including corn, wheat, rye, or rice in any form, whether as bread, cake, toast, zwieback, crackers, cookies, or breakfast cereals. Potato is prohibited. Sugar is forbidden as sweetening or in the form of candy, pastries, breads, etc., as well as dextrins such as are found in corn syrups and lollypops. Milk per se is not allowed.

The strictness of this diet cannot be over-emphasized, nor should the difficulty of adhering to it be minimized. Faithful observance requires intelligence and vigilance on the part of the mother or the person taking care of the child with celiac disease. It is surprising how many times a child will, despite the best parental supervision, manage to get hold of forbidden food. It is equally surprising how many parents of apparent intelligence will, despite all warnings, decide that "just a taste" of ice cream, cookie, or candy will do no harm. Nevertheless, treatment is best carried out in the home, with frequent visits to the doctor's office. Of the cases reported here, only 2 were hospitalized.

At the beginning of treatment, the patient is put on a so-called basic diet:

- BREAKFAST: Pot cheese, bananas, protein milk.
- LUNCH: Meat, pot cheese, bananas, protein milk.
- SUPPER: The same as lunch; gelatine may be added to any meal.

Any of these foods may be used in any quantity or given between meals.

After one week, orange juice, other cheeses, and egg may be added, one at a time and with a sufficient interval to test the acceptability of each. After two weeks all fresh fruits may be tried in the same way. When stools are controlled, vegetables (except potato) may be added; sometimes they are well tolerated but often their introduction must be postponed. Tolerance is eventually attained, at which time the diet is complete.

If, at the beginning of treatment, there is clinical evidence of gastrointestinal hyperactivity such as colic or vomiting, as is frequently the case, this may be controlled by suitable doses of atropine.

Most cases begin to improve immediately. The earliest sign of improvement is a change in the child's disposition; he becomes happy, smiling, contented. The diarrhea is often controlled in the first week, but in some cases such control may take a few months. His appetite improves if he suffered from anorexia, and he begins to grow and gain weight. During the first period of six months or more, any infection, especially in the upper respiratory tract, may be accompanied by a recurrence of the diarrhea. Also in this period the ingestion of a forbidden carbohydrate will bring about loose stools within hours or days, but the attack will quickly subside if no more of the forbidden carbohydrates are ingested. A break in the diet after about six months will not usually be reflected immediately in diarrhea, but the ingestion of forbidden carbohydrates must be continued for some time, even weeks, for diarrhea to recur. Otherwise, there are no relapses or so-called crises or catastrophes such as those described in much of the literature on the subject, requiring therapy to combat acidosis and dehydration.

Duration of treatment is of utmost importance. The strict celiac diet must be continued for at least one year. If there has been no recurrence of symptoms, forbidden carbohydrates may be added: one slice of bread three times daily, or a bowl of cereal once and bread twice; or cereal at breakfast, toast for lunch, and spaghetti for supper. If these additions to the diet cause no diarrhea, then potato is given. After three months with no disturbance, plain milk is added, and if no diarrhea occurs in the next three months with these additional foods, the patient may be considered cured, and all restrictions on the diet are lifted. As a rule, the entire cure requires no more than eighteen months, but when the diet has not been rigorously followed, it may take a much longer time.

When cure is obtained there should be no relapse. A striking example of the persistence of the disease in a case where the proper diet was not followed is given by one of our patients who was treated up to the age of 6 years. We were unable to get the child to follow the proper regimen because her mother owned a candy store and it was impossible to keep the patient from forbidden carbohydrates. At the age of 22 years she returned to us with all the symptoms she had had in childhood, and which had existed through the years. Placed on a strict celiac diet, which she followed faithfully, soon all symp-

toms had disappeared. She is now, eighteen months later, apparently cured, although not yet on a full diet.

Among milder cases of celiac disease there is a degree of tolerance for carbohydrates which allows for careless treatment with fair results, but cure requires two or three times as long as would be the case if a strict celiac diet were followed. In some such cases the symptoms are little relieved but physical progress is maintained so as to obscure the fact that a cure has not been obtained. Fortunately, time eventually seems to help these cases to get well, although many of them go through life with a tendency to loose stools.

THIS diet differs, in varying degrees, from all those previously advocated in literature on the subject. The basic difference is that our diet excludes *all* carbohydrates except those in fruits, in some vegetables, and in protein milk. Many other diets prescribe low carbohydrates but fail to specify the type of carbohydrate. This designation of the proper type of carbohydrate to be fed is of the utmost importance, as experience in the above cases shows that even the smallest quantity of the forbidden carbohydrates will precipitate diarrhea.

Since the common factor to be found in all fruits appeared to be levulose and glucose, we were led to try any food in which these occurred. Thus honey and dates were used and found to be fully tolerated.

To test the hypothesis that levulose was a satisfactory form of sugar in celiac disease, we obtained a supply of pure levulose through the Sugar Research Foundation, from the University of Colorado. We took a group of children suffering from celiac disease whose diarrhea and other symptoms were controlled, and whose progress was satisfactory. They showed recent histories of diarrhea for a day or two following the accidental eating of a lollypop, bread, cookie, or other forbidden carbohydrate. To these children we gave levulose daily in liberal quantities. In every case we found that it could be taken without ill result.

Many diets put forward in standard works on celiac disease restrict the use of fat, ascribing the cause of the disease to both fat and carbohydrate intolerance or to fat intolerance alone. The evidence behind such beliefs is the frequent occurrence of steatorrhea in the disease. But it

has been shown that fat is found in the stool even in a fat-free diet; and our experience in the 370 cases treated is that fat does not incite diarrhea. All our cases were fed fat in reasonable amounts during the course of treatment. When the whole dietary is low, fat must be somewhat restricted as it would be in the feeding of normal children; when proteins and carbohydrates derived from fruits are increased in the diet, fat may be taken in usual quantities. It should not be considered as a restricted food. Its absence from the diet is probably a contributory cause of rickets in many cases reported.

Many diets used in celiac disease call for the use of protein milk but fail to specify the type of protein milk. Many modified forms of protein milk have been devised, but our series of cases indicates that the only satisfactory product is protein milk prepared according to one of the three methods given earlier in this article, or calcium caseinate milk, in all of which the sugar content is low. All others should be avoided.

Although the above dietary regimen is the basis of treatment in the cases analyzed below, other modes of therapy have been considered and some of them tried; they should, therefore, be mentioned briefly:

*Vitamin B complex and liver extract*—From histories of our own cases and from literature on the subject, it is found that injections of these substances will in many cases end diarrhea for a variable period of time. But diarrhea usually recurs when such injections are stopped. This treatment is painful and disliked by patients.

*Antibiotics*—The use of antibiotics is usually followed by cessation of diarrhea, but it will recur after a period even while the antibiotic is still being given.

*Pancreatic extract*—It is not often used by us because dietary treatment gives the desired results. There are rare cases in which the addition of pancreatic extract seems to help.

#### PROGNOSIS

Under the dietary treatment described above, prognosis is excellent. Practically all cases recover and there should be no deaths.

A most important prognostic conclusion from the cases reported here is that in most cases cure can be effected within eighteen months,



and the acceptance of a slight diarrhea for four or five years until the child "outgrows it" is fallacious and harmful to the patient.

Our series indicated that with proper therapy pulmonary involvement is unusual and rarely fatal, that there need be no stunting or permanent mark of the disease. No avitaminosis was seen in any of our cases; rickets did not occur, chiefly we believe, because fats were not excluded from the diet.

Before the present mode of treatment, the prognosis of celiac disease was bad. In 1888, Gee said death was a common end. Even in 1927 Lehndorf and Mautner thought the prognosis was so hopeless that treatment was of little avail. Other reports on mortality were as follows: 1909, Heubner, 10 per cent; 1918, Heubner again, 14 per cent; 1921, Lichtenstein, 22 per cent; 1923, Hablutzal-Weber, 23 per cent; 1924, Pipping, 50 per cent; 1926, Schaap, 11 per cent; 1929, Hess-Thaysen, 22 per cent; 1932, Parsons, 10.6 per cent; 1935, Neale, 12 per cent; 1939, Hardwick, 36 per cent.

In addition, Hablutzal-Weber found in 1923 that 40 per cent of his living patients were below average in physique. Schaap in 1926 felt that if his patient recovered, he always bore the traces of his illness.

#### ANALYSIS OF CASES

OVER a period of some twenty-five years we have seen 603 children in whom the diagnosis of celiac disease was made. Of this total, 233 were not seen frequently enough or for a sufficiently long period to evaluate either the therapy used or the results. Of this number, 90 cases were seen but one time only as consultations referred to us by other physicians. The 143 remainder were seen only a few times for a period of less than 3 months each, before being lost track of for various reasons. (Table 1.)

Of the 370 cases adequately followed over a

TABLE 1  
TOTAL NUMBER OF CASES—603

Male .....	333 (55 per cent)
Female .....	270 (45 per cent)
Treated .....	370
Seen only briefly .....	233
Of 233 cases seen too briefly to evaluate:	
90 were seen only once as consultations referred to us by other physicians	
143 were seen only a few times during a short period and lost track of for various reasons	

period of some length, 270 or 73 per cent were cured, 89 or 24 per cent are recent cases still being treated and are on the road to cure; 8 or 2.2 per cent were not cured, and 3 or 0.8 per cent died. Cured cases are here considered as those patients who tolerate a full normal diet at the end of an arbitrarily established period of three years. (Table 2.)

TABLE 2  
TOTAL NUMBER OF CASES TREATED—370

	NUMBER	PER CENT
Cured .....	270	73
Under treatment .....	89	24
Not cured .....	8	2.2
Died .....	3	0.8

Data as to the length of time between onset of the disease and first treatment by us are available for 232 cases. In many of these cases diagnosis was made before we saw the patients. (Table 3.)

TABLE 3  
TIME BETWEEN ONSET AND FIRST TREATMENT BY US—232 CASES

Under three months .....	53
Three to six months .....	38
Six months to one year .....	47
One to two years .....	53
Two to three years .....	13
Three to four years .....	15
Four to six years .....	10
Six to seven and one-half years .....	3

Cases not cured are those patients who were unable to take a full diet at the end of three years. Of these 8 failures, 4 patients refused to follow the diet strictly and persistently; 1 was finally cured after four and one-half years; 1 was cured after six years; 1 suffered a relapse after asthma; and 1, who had regularly eaten potatoes from the early months of treatment, now has loose stools whenever excessive amounts of candy or cake are eaten. (Table 4.)

TABLE 4  
TOTAL NUMBER NOT CURED—8

Diet not followed .....	4
Cured after 4½ years .....	1
Cured after 6 years .....	1
Relapse after asthma .....	1
Occasional loose stools .....	1

The summary of those patients who died is as follows:

1. E. G. was first seen on December 7, 1925, at 16½ months of age, and hospitalized; gained 1½ pounds in first week, then acquired a ward infection of influenza and died of bronchopneumonia at the end of the second week of observation, December 20, 1925, having been under observation only thirteen days.

2. J. B., child of a physician, first seen on October 18, 1943, at 3½ months, died nine weeks later of acute tracheobronchitis, December 25, 1943, after a few days illness.

3. R. B. was first seen on August 27, 1937, at 15 months of age. He grew 6¼ inches and gained 7 pounds in the next fifteen months. At the age of 31 months he became ill with a pulmonary infection and died after four weeks, January 30, 1939, of empyema, pericarditis with effusion, and extensive pneumonia.

Of the cured cases, the age of onset of the disease was ascertained for 237 patients, as shown in Table 5.

TABLE 5  
AGE OF ONSET, CURED CASES—237 CASES

	NUMBER	PER CENT
Onset at birth .....	38	16
2 days to 6 months .....	59	25
6 to 12 months .....	89	37.6
1 to 2 years .....	38	16
2 to 4 years .....	11	4.6
Over 4 years .....	2	0.8

The time at which diarrhea was completely controlled is known for 189 of the cured cases. (Table 6.)

TABLE 6  
TIME OF CONTROL OF DIARRHEA—189 CASES

	NUMBER	PER CENT
Within 1 month .....	36	19
2 to 5 months .....	88	46
6 to 10 months .....	51	27
11 to 14 months .....	11	6
15 to 24 months .....	3	2

Our figures showing the length of time between the beginning of treatment and toleration of a full diet are based on 231 cases, as shown in Table 7.

All cases whenever seen were carefully checked not only as to whether the diet given was as directed but also whether any additional sub-

TABLE 7  
DURATION OF TREATMENT BEFORE TOLERATION OF  
FULL DIET—231 CASES

	NUMBER	PER CENT
Less than 1 year .....	27	11.7
12 to 18 months .....	104	45
18 to 24 months .....	58	25.1
24 to 30 months .....	24	10.4
30 to 36 months .....	7	3
36 to 42 months .....	7	3
42 months to 6 years .....	4	1.8

stances such as candy, cake, or bread had been ingested even in minute amounts. In a large number of these cases it was definitely shown that ordinary forms of carbohydrates given in small amounts produced diarrhea. This statement is based on the frequent observation that a child with celiac disease treated by means of the specific carbohydrate diet for an adequate time, who had formed stools, who was eating and growing well, had suddenly developed diarrhea for a short period. Upon investigation it was learned that a very small piece of bread, a single lollypop, a teaspoon of ice cream, or a cookie had preceded the diarrhea by a period of six to twenty-four hours.

It was also noted in this series that soon after the institution of the specific carbohydrate diet the first improvement noted was in the behavior and disposition of the child. The stools become less frequent and more formed, and a diuresis may occur. If there has been a clinical edema, this disappears with concomitant weight loss.

THE excellent results shown in these figures indicate that patients with the disease can be cured completely and that they will not relapse or show residual physical defects. The proper treatment for celiac disease is clearly shown to be the specific carbohydrate diet described above.

#### HYPOTHETICAL CONSIDERATIONS

Can any conclusions be drawn from the empirical finding that carbohydrates other than those found in fruits and to a lesser extent in vegetables will precipitate diarrhea? It may be helpful if we can discover the difference between these carbohydrates and others. Despite the fact that data on the analysis of specific carbohydrates in fruits are variable and often contradictory, it is probable that most fruit and

vegetable carbohydrates are monosaccharides, levulose and dextrose, while the carbohydrates that produce diarrhea are polysaccharides—lactose in milk, sucrose, dextrans, etc. We have postulated the theory, therefore, that the monosaccharides are completely utilized and well tolerated but that the polysaccharides not only fail to be utilized but actively incite diarrhea; that withdrawal of polysaccharides from the diet will see the cessation of diarrhea, and their absence for a sufficient time will see the return of the ability to utilize them. Further investigation of the composition of fruits and vegetables may throw valuable light on this theory.

Many questions are not answered by this hypothesis, of course, and it may be worth while to mention some of them to suggest lines of inquiry. In celiac disease we may be dealing with a relative tolerance of monosaccharides and polysaccharides. An individual case may have a specific threshold of tolerance for polysaccharides; a given small amount may be ingested without inciting diarrhea, but more than that may cause trouble.

The use of casec (calcium caseinate) milk may throw some light on this question. Our experience shows that a quart or more a day of casec milk may be ingested without the occurrence of diarrhea. One quart of casec milk contains the amount of lactose found in one pint of whole milk. Clinical experience proves, however, that one pint of whole milk will cause diarrhea. This dilemma suggests two questions: (1) Does casec milk fail to produce diarrhea because of the dilution of the lactose, or (2) because the lactose of the casec milk is split into its component monosaccharides when the milk is boiled with the protein calcium caseinate? Laboratory investigation will provide the answer to the second question.

Another problem is presented by the tolerance of banana in the celiac diet. The starch content of fully ripe banana is given as 1 per cent. Assuming that a celiac patient is fed ten bananas a day (as many of them are), he will ingest approximately 10 gm. of starch. But the feeding of 10 gm. of starch in the form of bread and cereal would be followed by diarrhea, which does not occur after the feeding of ten bananas. Is the starch found in bananas different from that found in cereal grains? We believe that it is. Examination of the stools of normal and celiac cases that are fed bananas shows large amounts of starch granules that stain blue with

iodine, indicating that the starch content of banana is encapsulated similar to a rice grain. These capsules of starch may pass through the intestine without becoming available for chemical reaction.

Hess-Thaysen's suggestion that sprue and celiac disease are identical points to another hypothesis which is worth investigation. As a result of our experience, we suspect that much of the recurrent diarrhea from which adults suffer is a mild form of celiac disease or sprue. We have treated a few adults with mild but persistent diarrhea with the specific carbohydrate diet with excellent results, but our figures are so inconclusive that they can do no more than suggest a fruitful line of inquiry.

Some theories concerning the etiology of celiac disease suggest themselves as a result of a study of our series of cases.

The action of forbidden carbohydrates in causing diarrhea leads to the deduction that they act as a laxative substance. But from a general physiologic point of view we know that increased speed of intestinal passage may be caused in at least four ways: (1) irritation from increased intra-intestinal bulk which speeds up motility of the gut; (2) hypertonic solutions; (3) substances stimulating the smooth muscle of the gut; (4) autonomic nervous stimulation.

If the deduction is correct that a lollypop, for example, acts as a laxative, then in which of the four ways does it do so? Certainly it does not increase the bulk of the gut content; it does not produce a hypertonic solution in the gut; there is no reason to believe that it affects the autonomic nervous system. We must then conclude that it is a substance that irritates the smooth muscle of the gut wall. Since there is no experimental evidence that carbohydrates per se are irritating to smooth muscle, we have considered the possibility that in the celiac case carbohydrate may be converted in the gut lumen into a substance which *is* irritating to the smooth muscle. Such substances as glucosides, which may be similar to the emodine cathartic group, suggest themselves in this connection.

IN considering the possible cause of such hypothetical conversion of carbohydrates, two possibilities suggest themselves: (1) that the intestinal enzyme systems of the celiac case are of such abnormality that instead of splitting poly-

saccharides into monosaccharides, levulose and dextrose, they produce the irritating substance; (2) that intestinal bacteria exist which produce such an irritant from polysaccharides. The latter theory is attractive when one recalls Herter's work on *B. bifidus* and *B. infantilis*.

This hypothesis that polysaccharides are converted into a laxative is compatible with many clinical findings in celiac disease. Rapid intestinal passage would cause deficient absorption of food elements and produce the steatorrhea of severe cases since there would not be time for the absorption of split and emulsified fats. Further, with insufficient absorption, a kind of internal starvation would result, reflected in such symptoms as loss of weight, failure to grow, malnutrition, anorexia, irritability, and asthenia.

The withdrawal of polysaccharides would eliminate the irritant substance which is laxative and thus stop the diarrhea, with the result that growth and good nutrition would be re-established. Polysaccharides could be introduced into the diet after a sufficient time because of (1) a readjustment of the enzyme system to proper splitting of carbohydrates, or (2) disappearance of bacteria from the intestine, depending upon the theory of causation held.

While this hypothesis does not fit all cases or explain all details, we have thought it worth suggesting with the idea that others may consider that it merits further investigation.

#### CONCLUSIONS

A study of our series shows that while the etiology of celiac disease remains obscure, a method of diagnosis and successful treatment has been found. A diet omitting all carbohy-

drates except those found in fruits and to a lesser extent in vegetables, and in protein milk, will cause symptoms to disappear, but they will recur if forbidden carbohydrates are ingested even in small amounts. This diagnostic procedure is simple and effective. The same diet will bring about a complete cure, without relapses, crises, or stunting, usually within eighteen months if the diet is followed strictly; somewhat longer if followed only half-heartedly. The diet which will effect this cure is specific in that it names the types of carbohydrates that may be used. A mere approximation of the diet outlined above will very likely bring unsatisfactory results. Strict adherence to the specific carbohydrate diet should bring complete cure.

#### SUMMARY

1. Celiac disease is a protracted, intermittent diarrhea of children caused by the ingestion of carbohydrates other than those found in fruits and to a lesser extent in vegetables and in protein milk.

2. The specific carbohydrate diet which cures celiac disease is based on the use of banana and protein milk, properly prepared, with the addition later of other fruits and some vegetables, plus meats, fish, fowl, eggs, gelatine, and natural cheese. Fats are given in normal amounts.

3. Symptoms disappear and nutrition progresses if this diet is followed strictly and forbidden carbohydrates are excluded. Cure results if this regimen is practiced for a sufficient time, usually eighteen months.

4. Of 603 cases reported, 370 were treated over a sufficient period to give conclusive results. All patients who followed the diet carefully for the required time were cured.

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