Celiac Disease

SIDNEY V. HAAS, M.D.
Peekskill, New York

THE EARLY HISTORY of celiac disease in the United States has never been written. Although Gee[1] had published his report in England in 1888, in this country the disease was quite unknown until the beginning of the present century when the late L. Emmett Holt, Sr., M.D., shortly after assuming the chair of pediatrics at the College of Physicians and Surgeons, Columbia University, called it to attention and tried to create an interest in the subject.

It is not generally known that the knowledge of the existence of such a condition and much of the progress made in the development of a successful therapy are directly due to Holt's influence. He animated three men: Christian A. Herter, M.D., Professor of Pharmacology and Therapeutics, a colleague on the faculty, and John Howland, M.D., and the author, two of his clinical assistants in the Department of Pediatrics at the Vanderbilt Clinic. The prognosis of celiac disease at that time was very bad, in part because only the severest form of the condition was recognized. The mortality rate was more than 50 per cent, and of those who did not die many remained stunted in growth in a state of semi-invalidism.

As the only survivor of those workers who participated in the early investigation of celiac disease, a short résumé of this phase seems desirable, not only for its present interest, but also for the future when the condition has been fully explored and properly evaluated.

This is not intended to be a comprehensive review of the subject, but rather an outline of the course followed in arriving at its present status, calling attention to the fact that the specific carbohydrate diet is also a completely gluten-free diet which has been used with utmost success for more than forty years in the treatment of the celiac syndrome.

Early contributions

HERTER. The first tangible result of Dr. Holt's effort was the monograph of Herter,[2] published in 1908, a study of 10 cases, all but 2 of which were contributed by Dr. Holt. The monograph attracted great and favorable attention, and for years Herter's infantilism became a synonym for celiac disease. It was an era when a bacterial etiology was sought, and under the influence of the times Dr. Herter was led to believe that the change in the intestinal flora was a cause instead of a result. He noted, however, that proteins were well borne, fats moderately, and carbohydrates very badly. He said:

> Carbohydrates are the obvious and fruitful cause of derangements of digestion, especially diarrhea and flatulence: in the severest cases the total quantity of carbohydrates which can be tolerated may be very small and supply less than one fifth of the calories required by an organism.

HOWLAND. The second result of Dr. Holt's influence was the important communication of Howland,[3] by this time professor of pediatrics at Johns Hopkins Medical School. In June, 1921, as his presidential inaugural address to the American Pediatric Society, Howland read a report in which the cause of celiac disease was attributed to the carbohydrates, and for its treatment he advised a carbohydrate-free diet. Dr. Howland's contribution was a great forward step. Although others had noted that carbohydrates were badly tolerated, he was the first to emphasize the import of the observation.

Howland's therapeutic results were the best up to that time. He stated:

> Of all the elements of the food, carbohydrate is the one which must be excluded rigorously; with this greatly reduced, the other elements of the food are almost always well digested, even though the absorption of fat may not be so satisfactory as in health. One would be hard put to treat these patients without protein milk.

The following are excerpts from the literature which tend to substantiate the thesis that the fault lies in the carbohydrates:

A deficit of lactase, maltase, or invertase may produce diarrhea profuse enough to arrest growth.[4] In 3 children with invertase or maltase deficit or both, diarrhea was arrested with a monosaccharide diet.[5] In an infant diarrhea disappeared promptly when the sugar concerned was omitted from the diet or if the lacking enzyme was added.[6] Diarrhea results from lactase deficiency.[6] Diarrhea was caused by a deficiency of sugar-splitting enzymes.[7] This form of diarrhea disappears promptly when the sugar is excluded from the diet or if the lacking enzyme is added.[8] In the production of celiac disease starches and disaccharides are only second to gluten.[9] In further substantiation of this viewpoint is the role played in celiac disease by gluten, a derivative of grain.

HAAS. The third direct result of Dr. Holt's influence was my own report,[10] read before the Pediatric Section of The New York Academy of Medicine in November, 1923, with the presentation of 8 patients cured by a diet from which carbohydrates, except those present in the banana, had been excluded. This practically solved the problem of the successful treatment of celiac disease.

Howland[3] had shown that cure could be obtained by the exclusion of carbohydrates from the diet, but he had met with almost insuperable difficulties when their reintroduction was attempted. These difficulties were overcome when it was found that the carbohydrate-rich banana was perfectly tolerated and apparently assimilated.

The result was so satisfactory that at first a specific factor in the banana was suspected of being responsible for the good effect. However, greater experience showed that in celiac disease all fresh fruits could be used, but owing to their inherent laxative property, it was necessary to restrict their use in the presence of diarrhea. Bananas, on the other hand, are not laxative and therefore possess a second unique value in the treatment of celiac disease.

In time it was possible to postulate that monosaccharides, such as levulose, glucose, present in all fresh fruits, dates, honey, and many vegetables, were well tolerated, whereas the disaccharides and polysaccharides, such as grain of all kind, flour, and other sugars, were not and, if used, would cause a return of symptoms.

ANDERSEN. In 1938 Andersen[11] called attention to a group of cases presenting the symptoms of celiac disease, all of which ended fatally. At autopsy there was a characteristic picture of cystic fibrosis of the pancreas and usually pulmonary involvement as well. Although Andersen was not the first to recognize or describe such cases (this had been done by Hess and Saphir,[12] Fanconi, Uehlinger, and Knauer,[13] and others), it was through her influence that these cases were established as an entity and separated from celiac disease. Despite this separation, these cases do better when given the specific carbohydrate diet in addition to the antibiotics, inhalations, pancreatic enzymes, and other measures which constitute the modern treatment of fibrocystic disease.

DIAGNOSIS OF *celiac disease usually depends on prolonged intermittent diarrhea. The following factors are important: role of carbohydrates; toleration of monosaccharides but not of disaccharides and polysaccharides, including grain; toleration of fats, even in presence of steatorrhea; autonomic imbalance, requiring use of anticholinergics; and value of fruit, especially bananas, in treatment of syndrome. In children, complete cure usually results after a year of adherence to the specific carbohydrate diet; in adults, in whom the condition is called sprue, relapses may occur, requiring a rigid diet for a few days or weeks.*

Factors in celiac syndrome

The disturbance of the autonomic nervous system in the celiac syndrome has long been recognized. Stimulation of the brain stem is capable of producing gastroduodenal lesions. The psychic irritability present in this condition may possibly find an explanation in this relation, although most cases are hypotonic and many are hypertonic, thus demonstrating the autonomic imbalance which exists.[14]

A pharyngeal spasm is shown by difficulty or inability to chew or swallow solid foods, pylorospasm by spitting and vomiting, intestinal hyperperistalsis by colic, and intestinal distention by gas. These symptoms are relieved promptly by supplementing the diet with adequate dosage of anticholinergics. Under the fluoroscope, when glucose is administered with the barium in cases of poor absorption, the intestines show clumping which disappears promptly after the use of Mecholyl.[15]

Contrary to the general belief, fats are not harmful in celiac diseases, despite the presence of steatorrhea which apparently is only a secondary manifestation and which

disappears under the specific carbohydrate diet when carbohydrate tolerance is reestablished. Fats may be used with impunity in the amounts usually taken, they have formed a part of the specific carbohydrate diet which has been used with success in the treatment of celiac disease for more than forty years. The laboratory lends support to this viewpoint. In 1921 and 1923 Schick and Wagner[16] demonstrated that there was an increased fat absorption when the fat intake was increased.

In 1957 Holt, Jr.,[17] showed that in celiac disease the more fat that is given, the more fat is lost in the stool, but also the more is absorbed. He stated that no change was observed in the percentage of absorption that could be attributed to the food, nor could it be discovered that the recovery was delayed by the liberal intake in any of the conditions capable of recovery. In 1949 Sheldon[18] reported that fat absorption was increased significantly when starches were withheld: "A starch-free diet resulted in dramatic improvement." The Haas specific carbohydrate diet cures celiac disease completely without danger of relapse. The patient is able to take all foods including gluten. He develops physically and mentally in a normal manner. There are no crises or deaths. All chemical and enzymatic processes connected with the digestion of fat appear normal.[19] All the unsaturated fatty acids are better tolerated.

This was the status of celiac disease in 1950 when Dicke[20] of Holland showed that gluten of wheat could produce the symptoms of the condition which would clear up if the gluten was omitted from the diet. His finding was hailed as a demonstration of the etiologic factor of celiac disease, a point of view which gained wide acceptance. However, time has shown that it is only one of the causes of the celiac syndrome, and although great improvement follows its omission from the diet, only a partial cure results, since most cases remain intolerant to gluten and relapse if gluten is used.

Sheldon and Simkiss[21] reported that of a group of patients who had been on a gluten-free diet for two years nearly 50 per cent relapsed when gluten was used again. There have also been reports of failures, crises, and occasional deaths. Patients in whom the gluten-free diet has failed have been cured by the specific carbohydrate diet and later are able to take gluten without ill results.

Dicke's[20] was the first scientific demonstration that an etiologic factor of the celiac syndrome existed in a carbohydrate, although it was in the protein fraction. All previous findings had been based on clinical experience and observation. Dicke's demonstration was an excellent achievement scientifically and of immense value for the study of the celiac syndrome, but clinically it was a possible disservice, since it ignored other carbohydrates as etiologic factors, although experience over the years had proved them to be so.

The diagnosis was largely dependent on the history of an intractable intermittent diarrhea, and the laboratory was able to furnish only negative evidence. With the laboratory data furnished by Van de Kamer and Weijers,[4] Weijers *et al.*,[8] Dicke,[20] and many others, this doubtless will all be changed and the subject finally clarified. The peroral gastrointestinal biopsies open up a vast field for future workers.

A single attack of diarrhea, no matter how prolonged, is insufficient justification for the diagnosis of celiac disease. The diagnosis is definite only if it is proved by a test of a carbohydrate-free alternating with a high-carbohydrate diet and if the diarrhea recurs on the introduction of carbohydrates. That the condition is outgrown is a myth which has scant basis in fact, although it may occur occasionally. What usually happens is that the individual accepts the frequent stools and the low average state of health as normal.

There are doubtless other causes which produce the symptoms of the celiac syndrome, but they play a very minor role. The celiac syndrome in the present state of knowledge is still of uncertain etiology, but preponderant evidence favors a carbohydrate intolerance. Practically all patients are cured by the specific carbohydrate diet, a cure which is permanent without relapse. This is not true when the exclusion of carbohydrates is incomplete, as in the so-called gluten-free diet in which a recurrence of symptoms is not uncommon with the reintroduction of gluten.

Specific carbohydrate diet

The specific carbohydrate diet, as used by us, is simple in principle. All fats and proteins are allowed, but carbohydrates are restricted as far as possible to the monosaccharides (levulose, glucose). It is a liberal diet which is easy to follow and can be varied easily to suit the demands of the patient.

The diet requires no special preparation except for the protein milk or an equivalent substitute. We have confined ourselves to casec (calcium caseinate) which is the casein of milk, purified and powdered.

Casec milk is prepared as follows (a double boiler simplifies the procedure):

Whole milk, not homogenized—32 ounces
Tap water—32 ounces
Calcium caseinate—8 level tablespoons

Mix the calcium caseinate and water and add to the milk in the inner vessel. Heat for twenty to thirty minutes, stirring occasionally. The inner vessel is then placed over the bare flame and brought to a boil, then removed from the flame. It is now finished. It may be sweetened with saccharin, sucrol, or similar sweetener. This gives 64 ounces, enough for two days; refrigerated, it keeps for days.

The following is the specific carbohydrate diet:

Proteins: All meats, with the fat, if desired. This includes ham, bacon, corned beef, and so forth. Gelatin (unsweetened) is permitted. All fish—fresh, boiled, broiled or fried; also canned—tuna, salmon, or sardines. All shell fish—crabs, lobsters, shrimp, and so forth. All cheese except processed; of the soft white cheese, pot cheese is the most satisfactory. Eggs in any form, sparingly.

Fats: All fats including oils and sour cream in amounts usually used.

Milk: None except protein milk or its equivalent; neither whole, skimmed, or the commercial so-called high-protein milk is acceptable.

Carbohydrates: All fresh fruits without exception; almost all vegetables except potatoes or corn; honey, dates, raisins, unsweetened fruit juices, in amounts depending on the frequency and consistency of the stool.

Foods absolutely prohibited:
All grain—anything containing flour (bread, cakes, and so forth).
All cereals.
All sugars except those present in fruits and honey.
All milk except protein milk or its equivalent.
All candies, pastries, ice cream, and similar sweets.

Bananas should be offered at every meal. They are the substitute for bread, potatoes, spaghetti, and so forth and can be used in any amount, fresh or dessicated, fried like potato chips, as pancakes, or combined with other fresh fruits as a salad. In the dessicated form bananas may be accepted, even though they are rejected as fresh fruit. Many palatable dishes can be made with the permitted foods.

Method

The specific carbohydrate diet must be maintained for at least one year, at which time it will be found that about 10 per cent of the cases are not yet ready to resume the use of carbohydrates but must continue the use of the diet for some months longer, rarely for six months.

Even though tolerance seems to be established much sooner, it is wise to continue the diet for a year when all carbohydrates are returned at one time. Except for the 10 per cent, all should show no bad reaction. If no adverse symptoms have appeared after three months use of carbohydrates, full milk replaces the protein milk, and if after three months more there have been no ill results, the patient may be discharged as permanently cured, without danger of relapse and able to tolerate all foods including gluten. This holds true for children but not for adults in whom the condition is called sprue. Although adults respond to the diet, relapses will occur, requiring a rigid diet for a few days or weeks. The condition has apparently become irreversible.

The material on which this article is based is from private practice. The patients usually come with the diagnosis of celiac disease for which treatment had been carried out for a long or short period of time. A careful analysis and follow-up of 603 cases substantiates the statements made in this paper.[22] The work of Weijers, Van de Kamer, and Dicke[5] and many others has been of great scientific value which, in time, should help solve the problem of the celiac syndrome.

The value of the clinic in the study of disease should not be overlooked and is well exemplified in celiac disease in which observation and clinical experience revealed the following facts: (1) the role played by carbohydrates; (2) that monosaccharides are tolerated, whereas disaccharides and polysaccharides, including grain, are not; (3) that fats are tolerated, even in the presence of steatorrhea; (4) that an autonomic imbalance exists in the condition, re-

quiring the use of anticholinergics; and (5) the value of fruit in the treatment of the celiac syndrome.

Summary

This is not a comprehensive review of celiac disease, but it recalls its early history in this country and shows the steps which led to the conclusion that the disease is due to carbohydrate intolerance. The laboratory has added further evidence of the validity of this viewpoint. Gluten as an etiologic factor, since it is a derivative of grain, also supports the conclusion of carbohydrate intolerance. This intolerance can be overcome completely and permanently by the use of the specific carbohydrate diet which happens also to be completely gluten-free. The gluten-free diet improves the condition but does not always cure. Relapses are common when gluten is restored to the diet, indicating that although it is an etiologic factor, it is not the only one. Only monosaccharides are tolerated; disaccharides and polysaccharides are not. The etiology is still obscure; the factor or factors exist in the carbohydrates. The importance of gluten, the protein fraction of grain, has already been demonstrated, but there are others which have not yet been revealed. Until our knowledge is greater, it will be necessary to exclude all carbohydrates, not only gluten, if a complete cure is desired. Although other etiologic factors may exist, they can only be of minor importance. Steatorrhea apparently is only a secondary factor which is cured simultaneously with the carbohydrate intolerance under treatment with the specific carbohydrate diet. Fats constitute part of the specific carbohydrate diet and are used from the beginning of treatment. Autonomic imbalance so frequently present requires the use of anticholinergics. Cure, according to our standard, means a return to normal health and development and the absence of steatorrhea, which must continue under a full diet including gluten, with no relapse ascribable to the condition. Children, when cured, do not have a relapse. Adults, in whom the condition is called sprue, although they respond to the diet as children do, have relapses at intervals. The condition apparently has become irreversible.

In this country L. Emmett Holt, Sr., M.D., was the first person to call attention to and to stimulate interest in celiac disease. There is a detailed description of the diet and the method of using it. The long course of treatment required by these patients makes them unsuitable for hospitalization. The patients on which this report is based were treated as ambulant cases, usually seen once a month. In the absence of pathognomonic symptoms, the diagnosis depended on the history of prolonged intermittent foul diarrhea, resistant to the usual treatment.

1879 Crompond Road

References

1. Gee, S.: On the coeliac affection, St. Barth Hosp. Rep. **24:** 17 (1888).
2. Herter, C. A.: On Infantilism from Chronic Intestinal Infection, New York, Macmillan Company, 1908.
3. Howland, J.: Prolonged intolerance to carbohydrates, American Pediatric Society, Tr. Am. Pediat. Soc. **33:** 11 (June) 1921.
4. Van de Kamer, J. H., and Weijers, H. A.: Malabsorption syndrome, Congress of Nutrition, September 1 to 7, 1960, Washington, D.C.
5. Weijers, H. A., Van de Kamer, J. H., and Dicke, W. K.: Malabsorption of Disaccharides, Series 24, International Congress of Gastro-Enterology, Leyden, April 20 to 24, 1960.
6. Holzel, A., Schwarz, V., and Sutcliffe, K. W.: Defective lactose absorption causing malnutrition in infancy, Lancet **1:** 1126 (May 30) 1959.
7. Blattner, R. J.: Diarrhea caused by deficiency of sugar-splitting enzymes, J. Pediat. **58:** 883 (June) 1961.
8. Weijers, H. A., Van de Kamer, J. H., Mossel, D. A., and Dicke, W. K.: Diarrhoea caused by deficiency of sugar-splitting enzymes, Lancet **2:** 296 (Aug. 6) 1960.
9. Von Heribert, B.: Die Differentialdiagnose des Coeliakie-Syndroms, Ann. paediat. **197:** 352 (1961).
10. Haas, S. V.: The value of the banana in the treatment of celiac disease, A.M.A. Am. J. Dis. Child. **28:** 421 (Oct.) 1924.
11. Andersen, D. H.: Cystic fibrosis of the pancreas and its relation to celiac disease, *ibid.* **56:** 344 (Aug.) 1938.
12. Hess, J. H., and Saphir, O.: Celiac disease (chronic intestinal indigestion), A.M.A. Am. J. Dis. Child. **48:** 1162 (Apr. 17) 1934.
13. Fanconi, G., Uehlinger, H., and Knauer, C.: Congenital cystic pancreatic fibrosis and bronchiectasis, Wien med. Wchnschr. **86:** 753 (July 4) 1936.
14. French, H. D., Porter, R. W., Cavanaugh, E. B., and Longmire, R. L.: Experimental gastroduodenal lesions induced by stimulation of the brain, Psychosom. Med. **19:** 209 (May-June) 1957.
15. May, C. D., and McCreary, J. F.: Glucose tolerance test in celiac disease; significance of low blood sugar curves, J. Pediat. **17:** 143 (1940).
16. Schick, B., and Wagner, R.: Concerning intestinal insufficiency in childhood, Ztschr. Kinderh. **30:** 223 (1921); **35:** 263 (1923).
17. Holt, L. E., Jr.: Observations on fat absorption in infants, Mod. Prob. Pediat. **2:** 85 (1957).
18. Sheldon, W.: Coeliac disease, Lancet **2:** 1097 (Nov. 26) 1955.
19. Weijers, H. A., *et al.*: Diarrhoea caused by deficiency of sugar-splitting enzymes, Lancet **2:** 296 (Aug. 6) 1960.
20. Dicke, W. K.: Celiac disease; investigation of the harmful effects of certain types of cereals on patients with celiac disease, Thesis, Utrecht, 1950.
21. Sheldon, W., and Simkiss, M.: Therapy and prognosis of celiac disease, Ann. paediat. **197:** 363 (1961).
22. Haas, S. V., and Haas, M. P.: Diagnosis and treatment of celiac disease: report of 603 cases, Postgrad. Med. **7:** 239 (1950).