

The Power of Observation in Advancing Celiac Disease

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ABSTRACT

The link between bread and wheat products and celiac disease was first recognized by Willem Dicke in the 1930s through clinical observations of his child patients. The role of gluten as the toxic factor was then proven by Drs. Dicke, Weijers and Van de Kamer in brilliant and prolonged studies in a small number of children.

The Dutch Coeliac Society helped us interview surviving child subjects of these studies.

Vignettes of their lives, difficulties and memories are presented in their own words. These testimonies emphasize the central role clinical observation has had in our understanding of celiac disease pathophysiology.

Key Words: celiac disease history, child research subjects, Willem Dicke

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THE POWER OF OBSERVATIONS IN ADVANCING CELIAC DISEASE

Celiac disease had been recognized for decades when, in the 1930s, Willem Karel Dicke, a Dutch pediatrician, observed that children with the disease relapsed when consuming wheat products but did well in their absence. He presented his observations and advocated for a wheat-poor diet in a manuscript in 1941 (1). The bleak war years prevented him from conducting the investigations needed to prove his clinical observations. Then, during the 1944 winter of starvation, when almost no bread was available in Holland, children with celiac disease improved markedly but relapsed quickly when white bread was parachuted into the country by allied airplanes. This further suggested the ill effects of bread products in celiac disease (2). Between 1946 and 1960, Dicke with Drs Weijers and Van de Kamer, finally performed the brilliant clinical research studies that proved the ill effects of wheat flour in children under their care. When these children relapsed from their disease, they were admitted to the Wilhelmina or Juliana Children's hospitals for months at a time. Initially, they were fed a flour-free potato diet to induce clinical improvement. Then they were observed when given diets containing wheat or wheat components (3). The purpose of these repeated studies was to define the toxic fractions responsible for symptoms and malabsorption. Before hospital discharge, they were fed a wheat-free diet again to eliminate symptoms and to increase weight toward normal. The pathophysiological link between wheat flour and celiac disease was based on dietary fat balance studies performed in 5 children and published in Dicke's PhD thesis in 1950 (4). The beneficial effects of the wheat-free diet in celiac disease were rapidly confirmed in Europe (5) and

What Is Known

- Clinical observations by an astute Dutch pediatrician suggested the ill effects of wheat in children with celiac disease in the 1930s.
- The toxic effects of wheat components and gluten on celiac disease pathophysiology were proven in repeated research studies in hospitalized children with the disease between 1946 and 1960.
- Conversations with surviving study children illustrate the difficulties faced by patients with celiac disease, their memories of the studies, and their attitudes to being research subjects.

the United States (6) and led to successful treatment of the disease with wheat-, and later, gluten-free diets and elimination of disease mortality.

Since these children contributed so much towards understanding and successfully treating celiac disease, we decided to contact them. We hoped to find out what they remembered, how they managed as they grew into adulthood, and what they felt about their participation in the research. They provide some insight into the extraordinary studies that formed the basis of our understanding of gluten and celiac disease pathophysiology.

THE CHILDREN'S VIGNETTES

JHB, born in 1944, one of the first children with celiac disease to be studied, was admitted repeatedly to the Wilhelmina Children's Hospital at age 2. She appears in Figure 1 among the children studied in the research ward. Upon discharge, her parents were told that she should avoid eating fat and spices but were given no other dietary advice. Into adulthood, she was often "low in energy and skinny" and suffered from anemia treated with frequent injections. When she got pregnant, physicians told her all should be fine, but she delivered a small-for-gestational-age baby. Aged 49, she had a myocardial infarction, was finally instructed about the gluten-free diet and has been well since. She questions why her family was never told to feed her a gluten-free diet but has no regrets about her participation in research.

HA was hospitalized at 9 months in a local hospital for over 3 years but was never diagnosed with celiac disease. Her physician suggested a diet of bananas and rice water, but her parents had

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FIGURE 1. Photograph of celiac disease subjects outside the research ward of the Juliana Pediatric hospital.

trouble paying for the special foods that were advised. Her siblings never accepted that she was sick, and she could not see them eat regular foods. During childhood, she needed repeated blood transfusions. She was diagnosed with celiac disease only at age 62. Her memories of hospitalizations were very positive. She would participate in future studies if that could help greater understanding of the disease.

TM, born in 1954, was an unhealthy infant. A friend suggested he might have celiac disease. TN was repeatedly studied in the hospital and was discharged on a gluten-free diet. He remembers that there was little understanding about the diet, only 1 shop sold gluten-free flour, and that many people felt that he was an attention seeker. His mother would make buckwheat pancakes when he went on a school trip to mimic the pancakes other kids ate. As a child, he had to collect stools for a week and was told that he had fat malabsorption. At 14 years, he was hospitalized to have a biopsy with a rubber tube. He thought he could outgrow celiac disease as an adult, stopped the diet, and had no problems until the age of 50 when the disease was rediagnosed “but very little pathology was found.” He had an appreciation for how physicians figured out the link between gluten and celiac disease and he would volunteer for future scientific research.

FC, born in 1953 in Amsterdam but moved to Curacao at age 3 months, was sick and skinny in infancy and improved somewhat when fed a banana diet. She was referred to Dr Dicke in Holland in 1956 and was diagnosed with celiac disease after studies in the hospital for 6 months without seeing her parents. There were 3 other children with celiac disease in the ward. One boy died. She was discharged with a diet of goat milk, raw liver, and small amounts of other foods. She members always being hungry. Her mother knew that she was a “guinea pig” and followed the physician’s instructions closely. She eventually was declared cured but was rediagnosed at over 50 years of age.

TN, born in 1946, had growth retardation and weight issues during the 1950s, her parents were advised to feed her a diet high in fat without much effect. She was not diagnosed with celiac disease until adulthood.

LI was hospitalized in 1956 for “a swollen abdomen, abdominal pain and diarrhea” and had repeated studies for 3–4 weeks every 2 months. She remembers a sweat test and was screened for leukemia by a sternum and hip biopsy. After numerous tests without a specific diagnosis, her parents arranged her discharge home. Her general practitioner suggested the possibility of celiac disease at age 6. However, it took another year for a specialist to first suggest she should have a gut biopsy after which she was treated with a strict gluten-free diet. She emphasized the lack of options for this diet and remembers her parents’ long search for buckwheat flour. She believes that too many tests were done to her as a child. However, she would participate in research studies on celiac disease now.

VOF was hospitalized for detailed studies at age 5. Throughout childhood, she always was tired, had a “full abdomen” and growth retardation and “would often take her younger sister’s place in the stroller.” She had a prolonged hospitalization, got many shots, and remembers not seeing her parents or 9 siblings for many weeks. After discharge, she started a diet of rice and bread from a special bakery. Subsequently, she was found to be lactose intolerant and was rediagnosed with celiac disease at a later age. She has no bad memories about her hospitalizations and would be happy to participate in studies going forward.

A NURSE’S MEMORIES

Complementing these personal anecdotes was the story of BN who, at 19 years, started working as a trainee pediatric nurse

in the research ward of the Wilhelmina Children's Hospital. She remembers that she had 5–6 children with celiac disease under her care that included some of the 5 research subjects described in Dicke's PhD thesis (4). The nursing team was aware that the patients with celiac disease were treated with special research diets. She remembers having to prepare porridges with varying grains. The children were hospitalized for 6 months at a time and were allowed to see their family weekly. She emphasized the role of Dr Weijers, who often decided on the composition of the children's diets.

CONCLUSIONS

What do these stories tell us about the child research subjects and their families? First, the remarkable resilience shown by these child research subjects in being repeatedly challenged with food items that made them sick. The faith of these families in their study physicians was still clear 70 years later. All would volunteer for research again. We heard about the lack of understanding about what celiac disease was and that it could only be treated with special gluten-free foods that were difficult to find and expensive. The children were accused of faking their illness to get attention and made to eat their meals apart from their siblings. As we hear these stories, we can understand the importance of the lay celiac disease societies that provided practical dietary advice and psychological support at a time that the disease was little understood.

Interestingly, some patients stopped their gluten-free diet as adults with few overt consequences, yet their health improved with gluten-free diets. Through the eyes of a pediatric nurse, we catch a glimpse of the environment in which Dicke and his collaborators tested the children with celiac disease. These studies were conducted before institutional review boards (IRBs) began to approve clinical research studies (7). We wonder whether such studies would be passed by an IRB today.

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