

HISTORICAL PERSPECTIVE

Treatment of Tropical Sprue: the Work of Dr. Bailey K. Ashford Examined in Retrospect

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Tropical sprue is a malabsorption syndrome that responds to treatment with folic acid and a broad-spectrum antibiotic. Eighty years ago, prior to the identification of the vitamins and the discovery of penicillin, clinical trials often consisted of best guess treatments based upon current knowledge and available technology. Dietary interventions were emerging as effective treatments for alleviation of diseases such as pellagra and beri beri. Representative of his generation of clinicians, Bailey K. Ashford, MD, one of the pivotal figures in academic medicine in Puerto Rico, carried out dietary studies in

his patients with tropical sprue. This historical retrospective presents an examination of the diets used by Ashford in terms of nutrient content and comparison to current recommended dietary allowances. Results show the diets to be inadequate for sustained nutrient value and especially low in folic acid. In summary, Ashford recognized the basic causes of tropical sprue but was unable to effectively treat the syndrome due to lack of adequate resources.

Key words: Tropical sprue, Bailey K. Ashford, Diets

Bailey K. Ashford, M.D. (1873-1934) was an important figure in the development of academic medicine in Puerto Rico. His autobiography, *A Soldier in Science* (1), chronicles his career as an army doctor who arrived in Puerto Rico at the time of the Spanish American war and stayed to spend the remainder of his life on the island as a practicing physician, first class researcher and community leader. He provided a driving force for the establishment of the School of Tropical Medicine, which evolved into the Medical School of the University of Puerto Rico. Justifiably, his memory is honored through a commemorative lecture series, which is now in its 42nd edition.

The objective of this historical perspective is to examine the treatment of tropical sprue as it was offered by Ashford in the light of present-day knowledge of the syndrome. We focus in the nutritional aspects of treatment using computerized data banks to analyze the composition of

diets recommended by Ashford for his tropical sprue patients and comment upon the adequacy and potential usefulness for offering alleviation from this malabsorption disorder. Comments on the development of modern day science are incorporated using Ashford's work as a lodestar.

Tropical Sprue – Then and Now

A recent review on malabsorption syndrome provides information on the current understanding of tropical sprue (TS) (2). "TS is a syndrome of unknown etiology that should not be considered a single entity. Patients must be suspected of tropical sprue if they are resident or were visitors in tropical or subtropical areas and have chronic diarrhea and malabsorption of two unrelated substances such as xylose and vitamin B₁₂. From a clinical point of view the condition is characterized by an overt malabsorptive state responding to folate and broad spectrum antibiotic treatment. Intestinal colonization with mixed fecal flora is observed and a role of protozoan parasites is increasingly demonstrated."

The existence of this disorder was recognized in India 2000 years ago and was first described in the medical literature in 1759 (3). The word "sprue" was first used in 1880 and by the turn of the century, clinical manifestations of what is now referred to, as TS were well recognized (3). Before the time of folate-antibiotic treatment there was

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considerable mortality from TS and while the syndrome is infrequently seen in Puerto Rico today, Ashford dealt with thousands of cases.

In the time of Ashford's work with TS patients in Puerto Rico (ca 1910-1930) the nature of the syndrome was very much more of a mystery than it is today and treatment was mainly a best guess, trial and error approach. To his credit Ashford and other investigators of his time were observant recorders of the syndrome and describe in detail the symptomatology and accompanying pathology of TS. A review of clinical aspects in the treatment of TS in Puerto Rico was the subject of a recent Ashford Conference (4).

In his report on the clinical investigation of tropical sprue (5) Ashford carefully documented salient features of the syndrome including its nature as being exposed to a tropical climate, involvement of hereditary and relation to previous wasting diseases including bacterial infection (*Monilia psilosis*). In other papers, Ashford focused on pathological consequences of TS including mycology of the intestinal canal and the anemias of sprue (6, 7) using examples of his own patients in case reports.

While it is now recognized that diet alone is not an effective therapy for TS (8), the first third of the 20th Century heralded the emergence of modern nutritional therapy as a state of the art remedy to the alleviation of disease. Indeed, this was the era of virtual elimination of such age-old scourges of mankind as scurvy, beri beri, pellagra and rickets in economically developed nations. Consequently, it became reasonable for researchers of the day to associate diseases with nutritional imbalance. The overall goal was to find just the right combination and quantities of corrective nutrients to alleviate the offending condition.

A hallmark of Ashford's work is the belief that sprue was due to a nutritional imbalance superimposed by bacterial infection. In a publication from 1916 (9) Ashford stated, of sprue: "In the absence of specific treatment, supervision of the diet appears to be the only available weapon we can turn against the disease."

From a treatise published in 1928 (7), Ashford elaborated on the pathogenesis of sprue:

"The outstanding contributive factor is excess of carbohydrates and fats in the food consumed and consequent diminution in the vital food accessories, as well as inadequate supply of certain amino acids. A relative failure of digestive glandular activity follows from overstimulation especially of the liver and pancreas and of the lipase and amylase function. The result is inadequate digestion of starch and fat, increase in

intestinal acidity and acid and gas producing micro organisms in a sugar-enriched medium; destruction of fat by bacteria; often a reduction of calcium content of blood serum and a progressive failure of nutrition."

While these concepts seem rather naive to the nutritionist of today, they occasionally are resurrected in the form of "fad diets" such as Atkins and Sugar Buster (10). In any case, Ashford implemented his nutritional therapies with the notion that the physician could gain cooperation of his patients through a reasonable explanation of the advised treatment (even though many seem almost impossible to maintain).

Dietary Treatment of Sprue

Depending upon toleration, one of 3 diets was recommended (9). These were: (1) The Milk Diet, (2) The Meat Diet and (3) The Fruit and Vegetable Diet.

The milk diet (9) consisted of feeding whole fresh milk as the only source of calories in portions beginning with 8 oz, 9 times per day for 4 days and to increase by one oz for each successive period of 4 days until 13 oz per serving was reached (a total of 6 periods or 24 days). Those who did not tolerate whole milk were advised to switch to skim milk. In addition, a modification for persons who "craved more food" included adding a banana beginning when 10 oz of milk was reached with an additional banana for each oz of milk above this amount. Consequently on the 24th day of the diet, daily consumption would be 117 oz (3.9 qt.) of milk and 4 bananas. Occasionally, oranges and grapefruits were substituted for bananas but pineapples, mangoes and alligator pears (avocados) were not allowed.

Nutritional analyses of the milk diet using either whole milk or skim milk and the modified diet containing bananas appears in the results section (Table 1).

The meat diet (8) consisted of feeding 2 lbs. of fillet chopped into 6 equal portions. Every 3 hrs a portion was served red after searing in a butter saucepan. 10 oz of hot

Table 1. Comparison of selected nutrients in diets used by Ashford in treatment of tropical sprue with current RDA values

Nutrient	RDA	Diet				
		Whole milk	Whole milk +Banana	Skim milk	Skim milk +Banana	Meat
Calories	2000	1897	1972	1082	1157	2002
% Fat	30	48.9	47.2	4.6	4.6	35.4
Cholesterol (mg)	300	420	420	56	56	373
Folate (µg)	400	154	170	161	177	222
Vitamin B ₁₂ (µg)	2	11	11	11	11	11
Fiber (g)	25	0	2	0	2	22

water or hot plantain gruel was provided along with saccharin sweetened coffee with milk (quantity not specified). The diet was modified after a week to use other types of meat (chicken, fish) or even fruits, vegetables or eggs.

Nutritional analyses of the meat diet appears in the results section (Table 1). Since specific amounts of coffee, fruits and vegetable are not provided, data analysis is restricted to the meat portion of the diet.

The fruit and vegetable diet (9) described by Ashford varied from bananas alone (15-20 per day) to a mixture of fruits and vegetables such as squash, eggplant, string beans, okra, tomatoes, spinach, cabbage, carrots, cauliflower, celery, cucumbers, leak, lettuce, onions, radishes, turnips and papayas. Since number and amount of these fruits were not given, no dietary analysis is possible so the fruit and vegetable diet does not appear in the results section.

It is curious to note that Ashford had very strong beliefs about the curative power of particular foods. In his view, bananas were far superior in nutritional benefit. None of the fruits and vegetables in the preceding paragraph had much food value but, according to Ashford (9) "when combined with bananas could be made to complete a fair diet of a temporary nature."

Dietary Analysis

The milk and meat diets and variations of these regimens were analyzed for nutrient content using the Minnesota Nutrition Data System 32 (NDS 32) which contains over 16,000 foods (11). It is a comprehensive nutrient database derived from USDA tables, food manufacturers, scientific literature and foreign food consumption tables, hence contains almost all foods commonly eaten in Puerto Rico.

Results

Diets analyzed were (1) the milk diet containing whole milk (4% fat), (2) the milk diet: whole milk + bananas), (3) the milk diet containing skim milk (0% fat), (4) the milk diet: skim milk + banana(s), (5) the basic meat diet.

Although complete nutrient analysis of each diet was performed only those components most related to TS are reproduced in Table 1. These include: total calories, percent fat, cholesterol content, fiber content, folate content and vitamin B₁₂ content. In Table 1, the column on the left represents recommended dietary allowances (RDA's) used for comparison of nutrient levels in the experimental diets (12).

A summary of nutrient content finds that the whole milk diet contains adequate calories and vitamin B₁₂ but too

much percent fat and cholesterol and virtually no fiber. Addition of banana increases the fiber slightly but has no other improvement. The skim milk diet with or without bananas has only about half the calories required. Fiber content is similar to whole milk. There is adequate vitamin B₁₂ but a very low percent fat and cholesterol content. The meat diet has recommended calories, fat and fiber and vitamin B₁₂. Cholesterol content is slightly high. A critical factor is the low folate content of all diets being only approximately half the RDA. Improvement of symptoms associated with megaloblastic anemia would appear very unlikely with any of these dietary regimens. Overall, these diets would have no immediate benefit and if prolonged could potentiate even greater nutritional deficiencies.

Furthermore it has been observed that in the later stages of tropical sprue, most persons develop an intolerance to milk due to a lactase deficiency (12). Hence, a milk diet would be impossible to completely digest.

Ashford continued recommending his sprue diet throughout the decade of 1920's (14, 15). His basic premise of high protein, low carbohydrate, and low grease was maintained but liberalization with added vegetables and fruits probably made the diets more palatable.

Discussion

When reviewing literature that first appeared 80 years ago, the reader cannot help but contrast the personalized narrative style in writing clinical cases by the authors of Ashford's generation to the epidemiology-correct case controlled or cohort studies of current authors. When Ashford proclaimed a TS patient "cured" or "improved," what criteria or end points did he use? How was compliance to his diets monitored? Where are the statistical analyses of his treatments? None of this information is provided. Yet, one should not expect to find it. The manner in which clinical trials were reported has changed (we hope for the better) since the first part of the century.

Ashford correctly recognized that sprue was a syndrome involving a nutrient imbalance superimposed by bacterial growth. His limitation in treating the disorder was lack of available resources. Widespread use of antibiotics waited future testing (penicillin was not discovered until 1930) and isolation of folate did not occur until ten years after his death.

How will scientific literature of today be judged 80-year from now? One would hope that the level of sophistication would be progressively advanced so that our generation of scientists would also seem competent and thoughtful, in short, to measure up to the quality exemplified by such individuals as Bailey K. Ashford.

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