OBSERVATIONS ON SKIN SENSITIVITY IN SPRUE PATIENTS

BEATRICE M. KESTEN and JENARO SUÁREZ
From the Department of Dermatology and the School of Tropical Medicine of Columbia University and the Presbyterian Hospital of San Juan, Porto Rico.

Intolerance to certain foods and the presence of Monilia psilosis (Ashfordi) in the alimentary tract of patients with sprue are two outstanding observations in the treatment and study of this highly complex disease. Weiss [1] has, in his recent survey of the literature and immunological investigations found no satisfactory explanation for this food intolerance. His work [2] included percutaneous tests with a variety of common foods. In that these tests were entirely negative he concluded that the digestive disturbances of sprue patients were not due to any specific food sensitization.

Skin tests with fungi of the monilia group have been somewhat more successful. Michel [3] demonstrated that the endotoxin of Monilia psilosis was capable of producing a local and focal reaction in sprue patients. He obtained positive skin reactions in sprue patients when he injected small amounts of a killed autolized suspension of Monilia psilosis subcutaneously. Controls gave negative or only slight local reactions which persisted less than twenty-four hours. Weiss and Landrón [4] repeated this work and also tested exotoxins (blood infusion broth filtrates) and a Cryptococcus isolated from erosio interdigitalis. These intradermal tests were done on a group of sprue patients and a control series of patients suffering from other diseases than sprue. A forty-eight hour reaction ranging from 1 to 4 plus was considered as positive. Twenty-two sprue and twenty-six control patients were tested with the endo and exotoxins of the above three fungi. Of the patients suffering from sprue fifty-four per cent (13 patients) gave a positive reaction to the endotoxin of the three fungi. Two additional patients reacted to one of the latter two fungi. Seventy-two per cent (16 patients) reacted to the exotoxin of all three fungi. One other patient reacted to Monilia psilosis and Monilia albicans, another to the Cryptococcus and a third to Monilia albicans and Cryptococcus. Of the controls nineteen per cent (5 patients) reacted to the endotoxin of the three fungi. One patient reacted both to Monilia albicans and Cryptococcus while another reacted only to the Cryptococcus. Fifteen per cent (4 patients) reacted to the exotoxin of all three fungi. All of the six sprue patients which

were tested with viable suspensions of the three monilia gave positive reactions as well as eleven of the thirteen controls.

Notwithstanding the above findings it was thought that the symptoms of sprue might be an expression of the hypersensitiveness of the mucosa of the alimentary canal to foods and fungi just as eczema and asthma have been found to be due to an increased sensitivity of the skin and respiratory tract to food and fungus allergens. With this in mind twenty-four patients with sprue, from the clinic of Presbyterian Hospital, were tested intradermally with a number of common foods and a few fungi. Nineteen of these patients presented the acute symptoms of sprue (inflamed, raw, sore tongue and mouth; profuse white frothy stools and loss of weight.) The remaining five have been under dietary and pancreatin treatment for sprue a varying length of time. They presented the glossy atrophic tongue and a moderate amount of gastro-intestinal disturbance.

FOOD TESTS

The solutions for food tests were prepared by extracting the dried or fresh food with n/100 sodium hydroxide or using Coca's[5] method, respectively, and then passing the solution through a Berkfeld filter. With the exception of sugar, the final dilution contained 1 mg. of nitrogen per 100 cc. 0.1 cc of the solution was injected intradermally. After ten minutes the tests were read. A test was considered positive if a wheal with definite irregularities like the pseudopods of an amoeba developed at the site of inoculation. These solutions included the following foods: beverages (coffee, cocoa); spices (achiote, anise, cinnamon, cloves, cumin seed, laurel, orégano, and peppers); cereals (corn, oats, rice and wheat); fruit (banana, orange, pineapple, strawberry); animal proteins (beef, chicken, pork, codfish, milk, egg); vegetables (apio, celery, batata, bread fruit, beans, plantain, potato, yautía and yuca); sugar and tobacco. These foods included fractional proteins as well as different varieties of the common proteins. These forty-three foods were tested on an average of eleven times (four to twenty tests on each of the twenty-four patients) making a total of about five hundred intradermal tests. All tests were negative with one exception. The one positive reaction was to kidney bean; this occurred in an elderly woman with acute sprue who did not eat beans because they did not agree with her.

In a dermatitis due to an external irritant, as in novocain or pyrethrum hypersensitivity, intradermal tests may be negative while the application of small amounts (patch tests) of the allergen to the skin surface will give a positive reaction thus demonstrating the

specific hypersentiveness of the epidermal cells. Similarly in sprue it was thought that because of the negative skin reactions it might be worth while to test the mucous membranes of the alimentary tract for hypersensitivity. The tests were similar to the intradermal tests except that the buccal mucosa of the lower lip was used instead of the arm. Six of the common foods (rice, beans, coffee, sugar, plantain and yautía), ones which are included and excluded in the sprue patient's diet, were tested on an average of three times (two to thirteen times) in each of sixteen patients with acute sprue. All tests were negative with the exception of one patient who reacted to rice and to the control (n/111 Sodium hydroxide with 5 per cent phenol.) The tests were repeated the following week and were negative.

FUNGUS TESTS

Ground, filtered extracts of cultures of Monilia psilosis, Aspergillus, and Alternaria containing 1 mg. of nitrogen in 100 cc of solution and the exotoxins of Monilia psilosis, Monilia albicans, and a Monilia isolated from a patient with erosio interdigitalis (Monilia 191) prepared according to the method used by Weiss [4] were tested on these same sprue patients and on thirty-two control patients suffering from either leprosy or pellagra. On the lateral surface of the upper arm 0.1 cc was injected intradermally. A reaction was considered positive if an irregular wheal with pseudopods surrounded by an erythematous area developed after ten minutes (immediate reaction) or an area of inflammation greater than 1.0 cm. with tenderness or local increase in temperature developed in from twenty-four to twenty-eight hours (delayed reaction.) The following chart shows the results of these tests:

Allergen	Patients with acute sprue			Patients with chronic sprue		
	No. Tested	Positive	Negative	No. Tested	Positive	Negative
Extract of ground:						
Monilia psilosis	13	8	5	4	0	4
Aspergillus	8	0	8	3	0	3
Altenaria	8	0	8	3	0	3
Blood Infusion Broth of:						
Monilia psilosis	11	2	9	4	0	4
Monilia albicans	12	0	12	4	0	4
Monilia erosio (191)	13	3	10	4	0	4
Control	16	0	16	5	0	5

All of the positive reactions occurred in patients with acute sprue and were due to fungi in the monilia group. The three patients reacting to endotoxin of Monilia erosio (191) and the two reacting

to the exotoxin of Monilia psilosis were among the eight reacting to extract of Monilia psilosis. Of these eight positive reactions one was of the immediate type, one patient gave both an immediate and delayed reaction and the remaining six were of the delayed type. With the exotoxin there was one immediate and one delayed reaction. The Monilia erosio (191) gave an immediate positive reaction in all three instances and one of these showed a delayed reaction as well. None of the patients reacted to: the control broth; the two saprophytic fungi; nor to Monilia albicans. Of the thirty-two control patients, one reacted to Monilia psilosis. This patient gave no history of having had sprue. All other tests were negative.

DISCUSSION

The entirely negative results of food tests confirm the findings of Weiss and Costa-Mandry [2] and substantiate the belief that food intolerance in sprue is not due to a hypersensitiveness to food proteins. Interpreting the positive reactions to the extract of Monilia psilosis as one would a positive tuberculin reaction it would suggest that about one-half of the patients with acute sprue show a hypersensitiveness to Monilia psilosis, i.e., they have or have had a monilia infection sufficiently severe to produce antibodies. About one-sixth of these patients also gave a positive reaction to the Monilia from erosio interdigitalis showing here as in the tests of Weiss and Landrón [4] that the tests are group rather than type specific. It is interesting to note that all of the positive reactions occurred in patients with acute sprue and that it is also during this stage that Ashford [6] finds Monilia psilosis in abundance in the alimentary canal.

SUMMARY

A series of twenty-four patients with sprue were tested intradermally with food and fungus allergens.

The food tests were essentially negative.

Eight of thirteen patients with acute sprue gave a positive reaction to an extract of Monilia psilosis. A lesser number of these patients also gave a positive reaction to blood infusion broth filtrates of Monilia psilosis (2 patients) and a Monilia isolated from erosio interdigitalis (3 patients).

ACKNOWLEDGMENT

The writers are indebted to Professors J. Gardner Hopkins and J. W. Jobling for the suggestion of this problem and to Dr. W. R.

Galbreath and the staff of the Presbyterian Hospital for their kindly cooperation, and to Misses E. Fruhbauer, R. W. Benham, and E. Brennan, and also to E. R. Squibb for the aid in preparation and supplying of a number of the allergens.

BIBLIOGRAPHY

1. Weiss, C.: Recent Literature on Tropical Sprue (1928) Am. Jour. Path., **6**: 885.
2. Weiss, C. and Costa Mandry, O.: Immunological Investigations in Tropical Sprue in Porto Rico. (V. Allergic skin reactions to various food preparations.) (1929) Jour. Imm., **16**: 283.
3. Michel, C.: A Study of Toxins and the Serological Reactions in Sprue. (1917) Am. Jour. Med. Sci., **154**: 177.
   Ibid: On the Use of a Monilia Vaccine in the Treatment of Sprue. (1918) Jour. Inf. Dis., **22**: 53.
4. Weiss, C. and Landrón, F.: Immunological Investigations on Tropical Sprue in Porto Rico. (1929) Am. Jour. Trop. Med., **9**: 83.
5. Coca, A. F. and Milford, A.: Studies in Specific Hypersensitiveness (XVII. The Preparation of Fluid Extracts and Solutions for Use in the Diagnosis and Treatment of Atopic Conditions). (1925) Jour. of Immunol., **10**: 555.
6. Ashford, B. K.: Studies in Moniliasis of the Digestive Tract in Porto Rico. (1915) Am. Jour. Med. Sci., **150**: 680.
   Ibid: Observations on the Conception that Sprue is a Mycosis Superimposed upon a State of Deficiency in Certain Essential Food Elements. (1922) Am. Jour. Trop. Med., **2**: 139.
   Ibid: Certain conditions of the Gastro-intestinal Tract in Porto Rico and Their Relation to Tropical Sprue. (1928) Am. Jour. Trop. Med., **8**: 507.