

SMALL INTESTINE ROENTGEN STUDIES IN FOOD ALLERGY*†

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THE study of gastrointestinal allergy has been handicapped by the lack of reliable objective diagnostic aids. Skin tests have been unreliable, elimination diets difficult and cumbersome to apply and often inconclusive. Special testing techniques involving the study of white blood cell counts before and after feeding of suspected allergens have failed to withstand critical analysis. Radiologic examination of the gastrointestinal tract incorporating test materials in the barium meal has been proposed as an objective diagnostic aid in gastrointestinal allergy.¹ The chief changes observed have involved the motor function of the stomach and small intestine and have consisted of (1) hypertonicity and, less frequently, hypotonicity of the small bowel, (2) hypermotility as evidenced by a rapid transit of barium from the stomach to the cecum, (3) segmentation of the barium column, and (4) at times delayed gastric emptying. These changes, however, are nonspecific and have been described in a variety of other disorders, including nutritional and purely psychogenic gastrointestinal ailments. The lack of specificity of these changes and the paucity of control studies have failed to inspire confidence in this technique. After a review of this field, Ingelfinger, Lowell, and Franklin² have suggested the following criteria for establishing the diagnosis of food allergy: "The food should be given in capsules or by stomach tube or in such a manner that the patient is unaware of its nature; reproducible symptoms, signs, or x-ray findings should consistently follow administration of the disguised food at a more or less constant interval, possibly not to exceed a few hours; other foods given to the patient in the same manner should not produce similar changes, and the suspected food given in the same manner to normal subjects should not cause the observed effects." The difficulty in fulfilling these criteria in clinical practice was recognized by these authors, who concluded that, "If the diagnosis could be firmly established in a number of cases, a characteristic pattern might become apparent and correlation with indirect tests might be possible."

An excellent and well-controlled study of the type just suggested was reported by Tallant, O'Neill, Urbach, and Price,³ utilizing the x-ray examination of the small intestine as a diagnostic aid in a group of patients with suspected food allergy. They studied 12 patients with gastrointestinal food hypersensitivity and first subjected them to x-ray study of the small intestine with a mixture of barium and water as a control after at least 5 days without ingestion of the allergen. These studies were essentially normal. Four or 5 days later, the x-ray study was repeated using, however, barium plus the suspected allergen for the test meal. All patients exhibited striking motility

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changes in the small intestine. One patient underwent a third study using egg to which he was not sensitive, and his small intestinal motility was found again to be normal. Eight nonallergic persons were tested in a similar fashion using milk, egg, pork, and corn, all with negative findings. Five food allergic patients without gastrointestinal disturbances were similarly studied and although their allergic complaints (neurodermatitis, asthma, and angioneurotic edema) were provoked by the test foods, no changes in the motility of the small intestine were induced. This report clearly establishes the value of x-ray examination of the small bowel in the study of food allergy and should answer many of the criticisms offered in the past. Further support for the usefulness of this technique has been presented by Schloss,⁴ who was able by Miller-Abbott balloon technique to confirm the production of motility disturbances by allergens introduced directly into the jejunum of 2 subjects whose x-ray studies had revealed striking motility changes after the feeding of the allergen.

In the present study, we have tried to evaluate the usefulness of the small intestine x-ray examination as an objective technique in 20 patients with suspected gastrointestinal food allergy. It was not possible to subject all of these patients to careful control studies but a few representative cases were so studied.

METHODS

X-ray studies of the small intestine were performed according to the technique described by Golden¹ using 4 ounces of barium sulfate in normal saline solution. Gastrointestinal motility was observed fluoroscopically and films were made at appropriate intervals. The features especially stressed were: (1) gastric emptying, (2) transit time of barium from the stomach to the cecum, (3) mucosal pattern, (4) tonicity (caliber of the lumen of the intestine), and (5) segmentation or lack of continuity of the barium column. Most of these patients were selected for this investigation because of histories suggesting food allergy with gastrointestinal manifestations. The latter consisted of flatulence, abdominal pain, and often diarrhea and nausea following the ingestion of specific foods. In 50 per cent of these cases, hives followed the ingestion of the offending allergen. Several patients exhibited marked eosinophilia but as a rule the eosinophil count was not elevated. A history of migraine was elicited in 7 cases. Four patients had experienced asthma. The commonest allergen was whole milk (70 per cent of the cases). Careful clinical and laboratory study excluded the presence of inflammatory, primary nutritional, parasitic, or neoplastic disease of the gastrointestinal tract in these patients.

RESULTS

The motility changes reported in the past^{1, 2} as manifestations of food allergy were encountered in 18 of the patients studied. In 2 patients, despite a history strongly suggestive of food allergy, no significant change could be demonstrated in small bowel motor function. The changes observed consisted of (1) hypermotility with rapid transit of barium from the stomach to the cecum in 14 patients (hypomotility was encountered in 4 patients), (2) hypertonicity of the small intestine, especially the middle and lower portions, and

(3) segmentation or discontinuity of the barium column. At times gastric emptying was delayed, but this was not a constant finding. These changes could be provoked by administration of the allergen during the course of the x-ray study and were often accompanied by symptoms of abdominal distress, cramps, and diarrhea. Elimination of the offending foods resulted in significant and often dramatic clearing of symptoms. The administration of antihistaminic drugs, among them elixir of Benadryl, Pyribenzamine, Neoantergan, and Perazil, was helpful in the management of acute symptoms and in the treatment of patients whose multiple sensitivities precluded the use of an elimination diet for any prolonged period. In some patients it was possible to allow small amounts of allergen in the diet providing antihistaminic medication was given. In a few, it seemed that food allergy disappeared if the patient were allowed to continue to eat the offending food while taking antihistaminic medication to minimize symptoms.

Of considerable interest was the observation that many patients exhibited motility changes in the small intestine before the allergen was administered at the time of examination. These changes, when present, were accentuated by feeding the offending allergen. In the past, it has been assumed that those changes might well represent the carry-over from previously ingested allergen. However, another theory is that the small intestine motility changes may be manifestations of an intrinsic or constitutional state of irritability of the small intestine (probably related to acetylcholine liberation) rendering the small intestine of these individuals peculiarly susceptible to the stimulus of various cholinergic trigger mechanisms, for example, histamine, chemical, bacterial, mechanical irritants, or psychogenic disturbances. This concept would be in conformity with the nonspecificity of the small intestine x-ray changes and it would also aid in the understanding of the findings just recorded. The food allergic patient may have a constitutional or intrinsic disorder of gastrointestinal motility rendering him peculiarly susceptible to the effects of various cholinergic stimuli. This may vary in severity from day to day and may account for some of the vagaries of food allergy. The attribution of the small intestine x-ray changes to cholinergic phenomena may also be helpful in understanding why identical changes may appear in those patients under psychogenic stress and when offending foods are ingested. The identification and elimination of offending foods or sometimes the administration of antihistaminics will relieve the symptoms in this group of patients and this may help to differentiate them from the purely psychogenic cases.

In illustration of the preceding discussion there are presented below several representative protocols of individual cases.

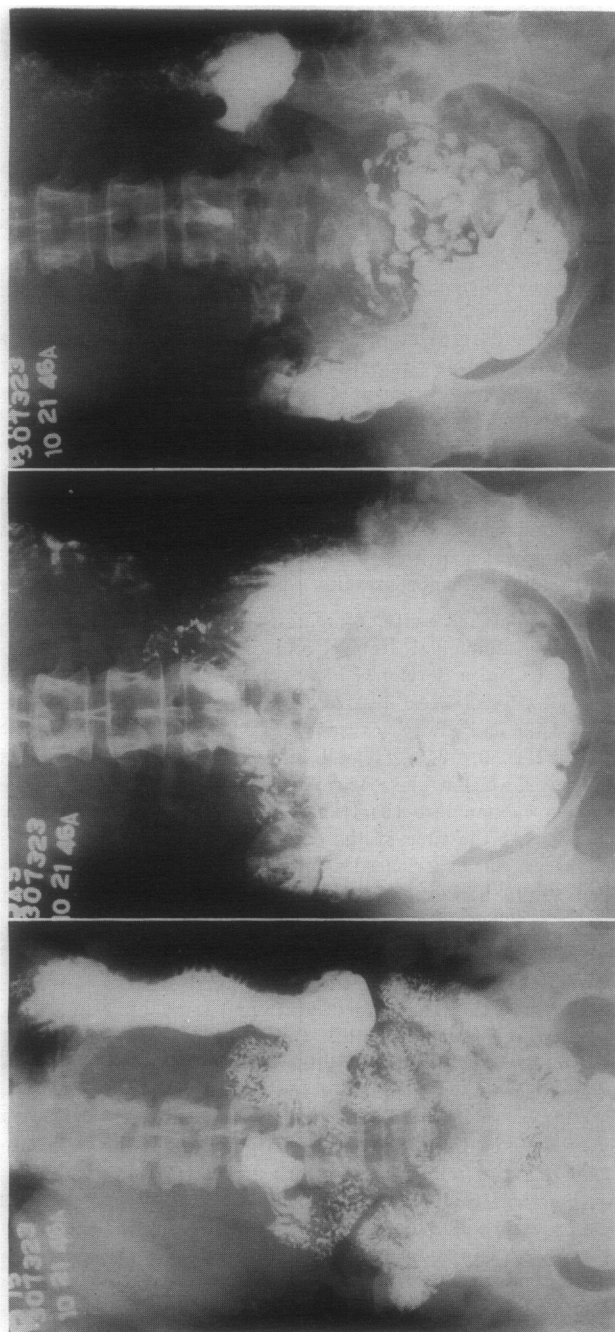
CASE 1.—A. M., a 41-year-old Cuban housewife, had for some years been troubled with flatulence, abdominal distress, and diarrhea following the ingestion of milk, eggs, or chocolate. She eliminated these foods from her diet and then, because of persistent symptoms, eliminated many others. When first seen by us in October, 1946, she presented the picture of severe malnutrition induced by a diet grossly deficient in proteins, calories, and minerals. The small intestine x-ray study on Oct. 16, 1946, revealed hypermotility and hypertonicity and segmentation of the mid-small intestinal region, interpreted as suggesting food allergy. On October 21, 1946, the x-ray study was repeated and again evidence was seen of hypermotility of the

small intestine, the barium suspension reaching the lower ileum within 15 minutes (Fig. 1). Fifteen minutes later, the patient was given an eggnog. This produced a violent reaction manifested by rapid propulsion of the meal into the sigmoid, markedly increased segmentation, and hypertonicity of the jejunum and ileum and diarrhea and abdominal cramps. Since it was evident from the clinical history that this patient was sensitive to a wide variety of foods, an elimination diet could not solve her problem, for adequate nutrition could not be maintained. She was consequently given elixir of Benadryl, 8 ml., before each meal and at bedtime, and encouraged to broaden her diet and to eliminate only the very worst offenders. During her hospital stay she was able, while taking Benadryl, to eat foods which in the past had produced much distress. She was examined again 1 year later, at which time she felt much improved and had gained 20 pounds. She was still taking Benadryl and was able to tolerate most foods except milk, which caused diarrhea unless it had been boiled.

CASE 2.—E. Z., a 50-year-old chemist, complained of diarrhea of 2 months' duration. He had known for years that milk caused considerable abdominal distress and flatulence. He was subject to ragweed hay fever. Careful studies failed to reveal any organic lesion of the gastrointestinal tract. A small intestine x-ray study on Jan. 20, 1949, revealed slight hypomotility, the barium column entering the cecum at 4 hours. At this time a glass of milk was given to the patient and this had a considerable simulating effect upon the intestine and within 30 minutes the barium column had passed from the cecum to the sigmoid and the lower ileum had become hypertonic (Fig. 2). He was advised to take elixir of Benadryl, 8 ml. before each meal, and to eliminate milk. The diarrhea stopped within 24 hours and subsequently he stopped using Benadryl but continued to eliminate milk. He then was free of diarrhea except on 2 occasions which he was able to attribute to corn bread and rye bread; these he eliminated from his diet with good results.

CASE 3.—D. G., a 40-year-old housewife, complained of abdominal distress, pain in the left lower quadrant, flatulence, abdominal cramps, and diarrhea, off and on for the past 7 years. During this time she had also developed hives and symptoms of allergic rhinitis. No organic cause for her symptoms had been discovered despite much study in several medical centers. She recalled that milk had always caused flatulence and at times diarrhea, so that she usually avoided it. On Dec. 9, 1948, a small intestine x-ray study revealed a slightly delayed transit time. However, after a glass of milk, considerable stimulation occurred, with rapid passage of the barium column into the transverse colon and marked hypertonicity of the mid-portion of the ileum. At the time of the examination, no symptoms occurred. However, about 7 hours later, the patient experienced a severe bout of abdominal distress, diarrhea, nausea and vomiting, and severe borborygmi. When seen by her local physician her blood pressure had fallen to 80/60. The episode cleared spontaneously within 48 hours and suggested to us a delayed allergic reaction to milk.

CASE 4.—T. Z., a 29-year-old clerk, complained of abdominal distress and diarrhea. During World War II he was stationed in the Pacific for 3 years and was unable to obtain whole milk and refused to drink reconstituted powdered milk. On returning to San Diego, Calif., in the fall of 1945, he was able to obtain a 5 gallon container of fresh milk daily for his outfit. He claimed he drank all of it himself, 5 gallons daily for 4 to 5 weeks! He gained 30 pounds and felt perfectly well. He was subsequently transferred to a post where milk was more difficult to obtain. Several months later, he was discharged and began work as a clerk in a grocery store. He drank 1 quart of milk while at work and developed abdominal cramps and diarrhea. The next day, the same thing occurred 4 hours after drinking milk. He consulted a physician who prescribed a low residue diet and advised him to continue the milk. However, the patient noticed that milk, even in small quantities, invariably produced abdominal cramps and diarrhea. The patient, therefore, decided to omit milk from his diet. However, he was still curious about this effect and decided to consult another physician, who also told him that milk could not be causing his symptoms and advised him to continue with it. However, the patient avoided milk until 1 day when he ate blueberries with a small amount of milk. One hour later he developed epigastric cramping pain followed by generalized abdominal distress and diarrhea which continued for 7 hours. He then consulted us and on Aug. 4, 1949,



A.

B.

C.

Fig. 1 (Patient A. M.).—The illustration on the left is of the film taken 15 minutes after the ingestion of barium. Fifteen minutes later the patient was given an eggnog, which produced a violent reaction with rapid propulsion of the barium meal into the sigmoid, markedly widened segmentation, and hypertonicity of the jejunum and ileum as demonstrated in the center film, taken 15 minutes after the eggnog, and the film on the right, taken 30 minutes after the eggnog.



Fig. 2 (Patient E. Z.).—The view on the left is at 4 hours after taking barium. Following it, milk was given by mouth, and it had a considerable stimulating effect on the intestine. Within 30 minutes, as seen in the center and right-hand illustrations, the barium column had passed from the cecum to the sigmoid and the lower ileum had become hypertonic.

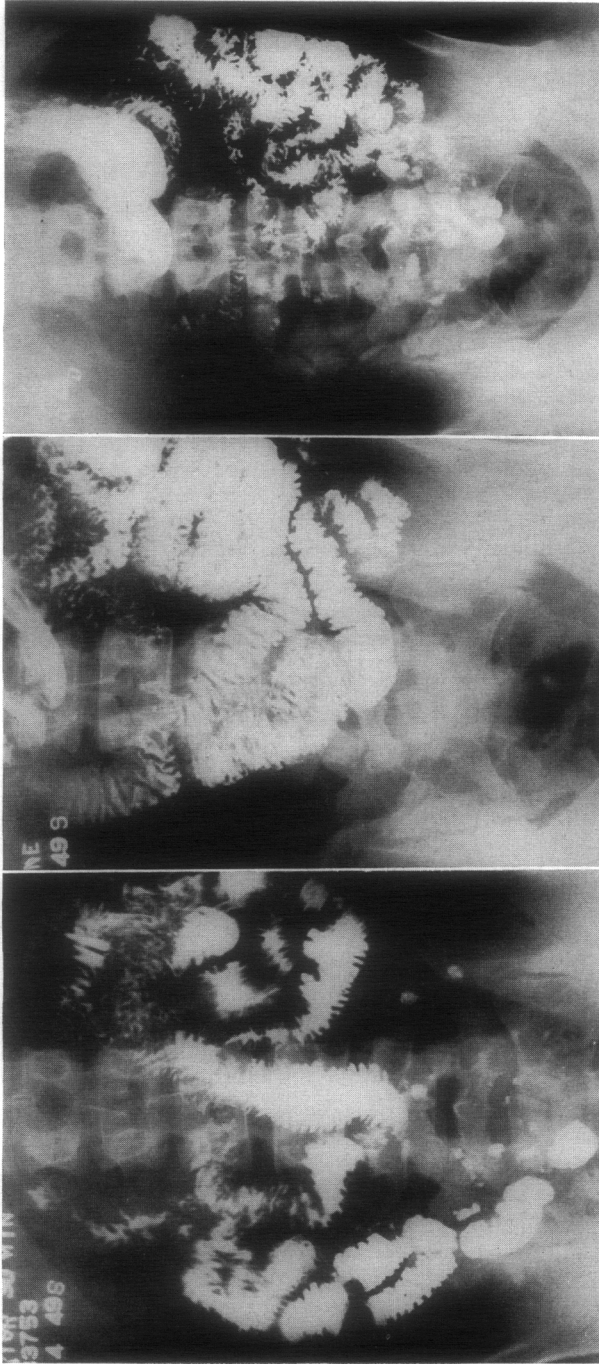


Fig. 3 (Patient T. Z.).—The illustration on the left is the 1 1/2 hour film of the study of Aug. 4, 1949, of this milk-allergic patient; it reveals a disturbance in motor physiology of the small intestine with widening of the folds of the jejunum and slight segmentation. The center view is the 1 hour film of the study of Oct. 26, 1949, after the patient had eliminated milk for 11 weeks and was symptom-free. The small bowel now appears normal. On Nov. 10, 1949, a repeat x-ray study was done, and at this time milk was mixed with the barium meal. The illustration on the right is the 1 hour film of that study and again there is evidence of small bowel motor dysfunction provoked by milk.

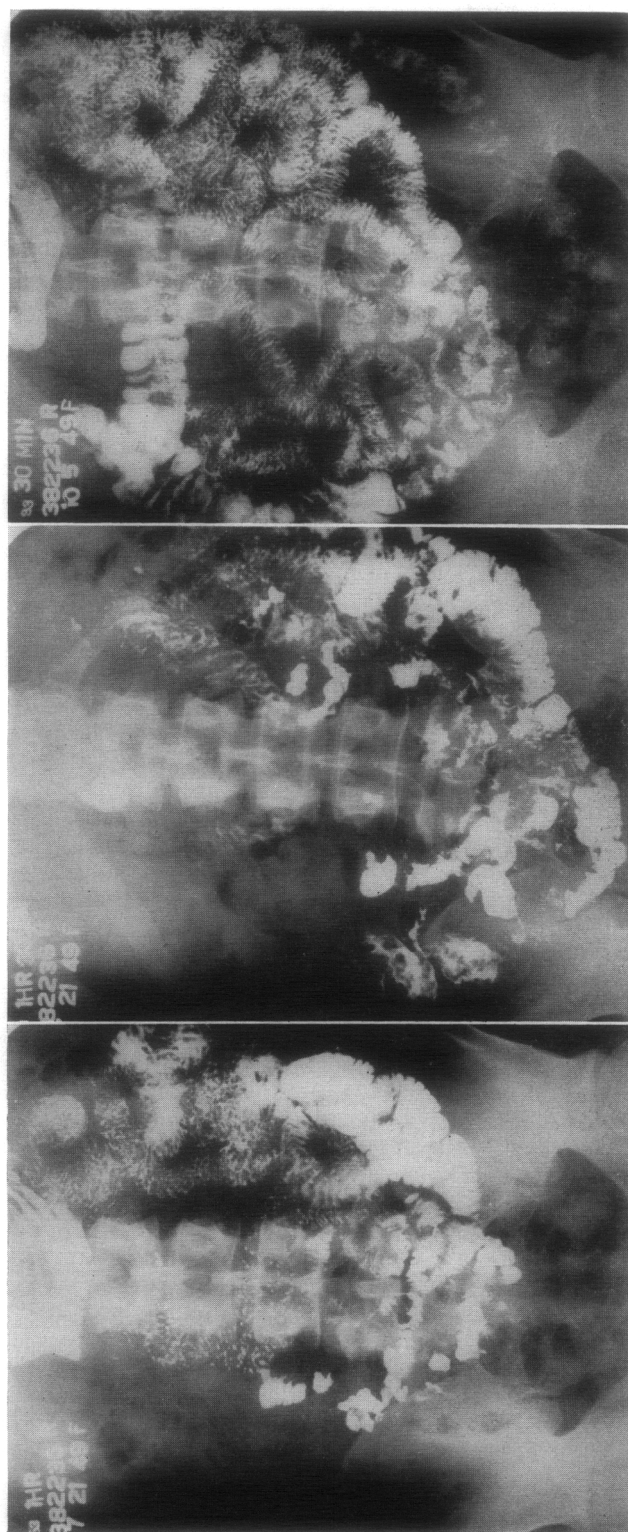


Fig. 4 (Patient C. K.).—Ulcerative colitis and milk allergy. The illustration on the left is the 1 hour small intestine film taken July 21, 1949, revealing a disturbance in motor function of the small intestine; this is accentuated in the center view of the 1 1/4 hour film. The patient was taken off milk. The repeat study taken on Oct. 5, 1949, seen on the right reveals in the 30 minute film an essentially normal small intestine with the exception of hypermotility.

a small intestine x-ray study was performed and it revealed a moderate disturbance in motor physiology of the small intestine manifested by widening of the mucosal folds in the jejunum and slight segmentation. There was, however, no appreciable immediate reaction to milk. The patient was placed on a milk-free diet and returned for re-examination of the small intestine on Oct. 26, 1949, at which time evidence of considerable improvement was found in the small intestine motor physiology (Fig. 3). The patient has avoided milk and has been free of symptoms up to the present.

In some of our patients the diagnosis of food allergy was entertained only after the motility of the small intestine had been reported as abnormal by the radiologist. Follow-up study of the patients was especially interesting, for it often revealed a previously unrecorded history of food sensitivity.

This is illustrated by the case of J. N., a 13-year-old feeble-minded boy who was brought to the clinic by his mother for investigation of diarrhea which had been present for some years. An adequate history was almost impossible to obtain because of the patient's mental retardation and his mother's low level of intelligence. A small intestine x-ray study revealed very striking changes in motility, present to a mild degree before giving milk and aggravated remarkably by the ingestion of milk. After this report was obtained, the history was checked with the patient's mother, who recalled that this child had always been different from her other children because milk had always "given him the runs." Without the x-ray study of the small intestine, the diagnosis would probably not have been suspected in this patient.

While the recognition of food allergy is of considerable importance in patients with uncomplicated gastrointestinal disturbances, it is of even greater significance in the patient with organic gastrointestinal disease to which it may be contributing. This is illustrated by the following protocol of a patient with nonspecific ulcerative colitis.

C. K., a 32-year-old merchant seaman, developed diarrhea and abdominal cramps in October, 1948, for which he was treated in the Marine Hospital, Staten Island, for 2 months, and the diarrhea subsided. In May, 1949, he had a recurrence of bloody diarrhea during which he lost 35 pounds. At this time he was living in a hotel room and subsisting on a diet consisting chiefly of milk despite the fact that milk had always caused him to have diarrhea in the past. Sigmoidoscopy on July 5, 1949, revealed severe and classical ulcerative colitis. A small intestine x-ray study revealed hypermotility, segmentation, and hypertonicity present to some degree before giving milk but markedly accentuated after giving milk (Fig. 4). Eosinophilia of 32 per cent was found but the remainder of the laboratory studies were negative. He was advised to stop milk and was given Neoantergan, 50 mg., before each meal and at bedtime. Within 24 hours the diarrhea had begun to lessen, and within 72 hours he was having semiformal stools. Improvement was dramatic and he quickly regained weight. His clinical improvement was accompanied by sigmoidoscopic improvement and within 1 month he was in a complete clinical remission.

He was seen occasionally and in March, 1950, he reported that after feeling perfectly well and gaining 30 pounds he had become involved in a violent family quarrel 3 weeks before and had almost immediately developed a recurrence of bloody diarrhea. He had eliminated milk and tried Neoantergan to no avail and had lost 36 pounds in 3 weeks. Again the sigmoidoscopic findings were those of acute severe nonspecific ulcerative colitis. He again had an eosinophilia of 19 per cent. Treatment consisted of Banthine,^{5*} an anticholinergic drug which has a selective action on the gastrointestinal tract. This induced a dramatic remission within 24 to 48 hours and this was well sustained so that within 5 weeks he had regained almost 10 pounds and was having 1 formed bowel movement daily without blood or mucus. The eosinophil count dropped gradually from 19 to 14 to 10 to 1 per cent by the fourth week of treatment.

*Banthine was generously supplied by G. D. Searle & Co., Chicago, Ill.

For some years Andreson⁶ has suggested that food allergy is responsible to a large degree for the illness called ulcerative colitis. The case just described could support this belief. However, in our experience, the striking sequence of events just listed has been the exception rather than the rule. It is of interest that in this patient the initial episode of colitis treated by us responded dramatically to an elimination diet and an antihistaminic. The second episode appeared to have been initiated by an emotional upset rather than an allergic stimulus and curiously enough, this attack was also accompanied by a high eosinophil count. Apparently a psychogenic cholinergic stimulus had reproduced the picture which 1 year before had been initiated by milk allergy. The beneficial effect of Banthine, an anticholinergic drug, was so striking that further investigation of this phenomenon has been initiated and will be the subject of a later report.⁷

SUMMARY

The x-ray examination of the small intestine in patients with food allergy affords an objective method which is useful in the study of this disorder. The motility changes are nonspecific and are found in a variety of conditions. They may, however, be modified in many instances by the withdrawal of allergenic foods or by the administration of antihistaminic drugs and by this means a degree of specificity may be achieved. The nonspecificity of these changes is comprehensible if they are viewed as results of cholinergic stimulation of an unstable or irritable autonomic nervous system. This may well be the common denominator in the response of the small intestine to allergens, mechanical, chemical, and bacterial irritants, and psychogenic threats. Further study is being made of this important point and this includes the further investigation of anticholinergic drugs such as Banthine.

The role of food allergy in the causation or aggravation of organic disease of the intestine, stressed by many and deprecated by others, has suffered because of the lack of objective methods of study. By the use of the x-ray examination of the small intestine, giving the suspected allergen in the barium meal, or during the course of the study, it has been possible to produce marked disturbances of motility in food-sensitive persons, in support of these clinical histories. This technique may be of considerable importance in the study of some patients with ulcerative colitis and other organic diseases of the gastrointestinal tract.

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