

# ABSORPTION OF WATER AND SODIUM FROM THE SMALL INTESTINE OF PATIENTS WITH NONTROPICAL SPRUE

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There is evidence that the absorption of water from the gastrointestinal tract of patients with nontropical sprue is delayed when they have recently eaten food (1) and also when they have fasted (2, 3). Excessive fecal loss of sodium has been demonstrated in patients with nontropical sprue (4), and recently evidence obtained by the use of isotopic sodium has indicated that the absorption of sodium chloride from the small bowel of patients with this disease is delayed (5).

The present study was undertaken to confirm, if possible, the presence of a defect in the absorption of water or sodium in fasting patients with nontropical sprue and to obtain a more exact measurement of its degree. The study was made possible by the recent development of a method that allows the precise quantitative determination of the rate of absorption of isotopically labeled substances from the gastrointestinal tract of human beings under completely physiologic conditions (6).

## METHODS

Fourteen patients who presented typical clinical, laboratory and roentgenographic features of nontropical sprue were studied. Three were men and 11 were women. Their ages ranged from 23 to 63 years with the majority being in the mid-thirties. Rates of absorption were determined in most of the patients on only one occasion, the majority of these being obtained during relapses of the disease. Six tests were made during remissions.

A designation of the clinical status of the disease in each patient at the time the tests were performed has been used. When loss of weight, abdominal discomfort and diarrhea or any combination of such features of the disease predominated, the patient's clinical status was termed a "relapse." When such features were absent, or nearly so, the term "remission" has been used. These terms are intended to provide only a very rough estimate of the severity of the disease in each of the patients at the time the test of absorption was made.

All observations were made in the morning. The patients had eaten nothing since the meal of the previous evening. In each test the isotopes were introduced into the upper part of the small bowel through a Sawyer tube after the position of the tube in the third portion of the duodenum had first been established by fluoroscopic examination. As a routine, about 10 gm. of barium sulfate was mixed with the test material and its distribution throughout the abdomen followed by frequent fluoroscopic and roentgenographic observation.

The tests made in the course of this study fall into two groups. In the first, the rate of absorption of water alone was measured; eight such observations were made on five patients. In the second group, the rates of absorption of both water and sodium were determined. In addition to the dual determinations, refinements in methodology developed during the progress of the second part of the study allowed more precise determination of the rates of absorption of both water and sodium.

The method (6) employed for estimation of the rate of absorption of a labeled substance requires determination of its rate of appearance in the arterial blood while it is being absorbed, as well as its rate of disappearance from the arterial blood stream after its rapid intravenous injection. The precise rate of absorption of the isotope is then calculated by integration of these two rates. In the past it has been necessary to employ mean rates of arterial disappearance of the isotopes as determined in a group of healthy persons (6-8), and this was the procedure adopted in the first group of observations presented in this report. While use of a mean rate of arterial disappearance has been appropriate for the study of normal human beings, since rates of arterial disappearance vary so little among healthy persons, it was recognized at the outset that it might not be as applicable to the study of patients who are sick. The first step toward correction of this weakness was to determine the rate of disappearance of each isotope following its intravenous injection a few days before, or after the determination of its rate of appearance in the arterial blood during absorption from the bowel. This procedure was adopted in four of the nine patients of the second series; a further improvement was made in the tests on the five remaining patients. In these, dual isotopes of water (deuterium and tritium oxide) and dual isotopes of radiosodium (sodium<sup>22</sup> and sodium<sup>24</sup>) were employed (9). One of the isotopes of each pair was given intravenously while

simultaneously the other of each pair was placed in the small bowel. Determination of the concentration of the isotopes in the same samples of arterial blood then yielded simultaneous appearance and disappearance rates for both water and sodium. These rates were then employed in the calculation of the rate of absorption of each of the isotopes. The procedures followed in carrying out these tests did not differ significantly from those followed when single isotopes were used (6). The methods followed in analyzing for the dual isotopes in the blood and the validity of the procedures were first established by experiments on dogs and then applied to tests on human beings (9).

The quantities of the isotopes used in the test ranged from 19 to 50 gm. of deuterium oxide ( $D_2O$ ), 2.5 to 3.0 millicuries of tritium oxide, 10 to 25 microcuries of radiosodium<sup>22</sup> and 14 to 100 microcuries of radiosodium<sup>24</sup>. The radiosodium was routinely dissolved in the labeled water and sufficient sodium chloride was added to make the solution isotonic. Zero time in the test was taken as the midpoint of the injection of the isotopes, those into the bowel being synchronized with those into the vein. Samples of arterial blood were drawn at minute intervals for 12 minutes and then less frequently until the termination of the test at 1 to 2 hours. Samples of blood for determination of the 3-hour or 24-hour equilibrium values were drawn by separate venipuncture. The concentrations of the isotopes in the blood were determined according to methods that have been described previously [deuterium with a mass spectrometer (10, 11), tritium with a liquid scintillation counter (12) and radiosodium in a well-type sodium iodide (thallium) scintillation counter].

Calculation of the rates of absorption of the isotopes was carried out according to the procedure previously described (6) except that in the last group of tests the time intervals used in the calculations were changed. The concentrations of the isotopes at  $1\frac{1}{2}$ ,  $3\frac{1}{2}$ ,  $4\frac{1}{2}$ ,  $5\frac{1}{2}$  minutes and so on, up to  $11\frac{1}{2}$  minutes, and the concentrations at 14 minutes and every 4 minutes thereafter up to 50 and then every 10 minutes for the remainder of the

first  $1\frac{1}{2}$  hours were employed instead of those previously reported. This represents a slightly different time scheduling from that employed previously in the calculation. The change has been found to improve the determination of the rate of absorption of sodium. Such rather minor factors have been brought into focus by elimination of the use of a mean disappearance curve and adoption of the more accurate procedure of using the disappearance curve belonging to each individual, particularly when this is determined at the same time as the test of absorption. The concentration of the labeled water in the venous blood 3 hours after its administration was used as the equilibrium value in the calculations. In the case of sodium, the concentration in the venous blood at 24 hours was used as the equilibrium value in the majority of the tests; use of a 3-hour to 9-hour equilibrium in a few instances did not significantly alter the results. In each determination the percentages of the isotopes absorbed as the test progressed were plotted, and the slope of the straight line that best fitted the points which included the absorption of at least the first 50 per cent of the isotopes was expressed as the initial rate of absorption; in addition, the time required for the absorption of the first 50 per cent and 67 per cent of the administered amount of each of the isotopes was recorded.

## RESULTS

### *Patients in whom absorption of water alone was tested*

In this group of tests a mean rate of disappearance of deuterium oxide from arterial blood as determined in a series of normal persons was used in the calculation of the rate of absorption. The results may be compared directly with those obtained previously in our laboratory with the same technic (6-8). We have calculated the mean values for the total of 29 healthy persons tested in

TABLE I  
*Group 1—Rate of absorption of water from small bowel of patients with sprue*

Case	Test	Initial rate, % absorbed per minute	Minutes required for absorption of		Clinical status
			50%	67%	
1	126	21.7	2.8	4.7	In remission
	113	13.5	4.4	6.4	In remission; relapsed 5 days later
2	119	7.1	6.8	12.8	In relapse
	125	7.8*	6.4	9.6	In relapse
4	112	10.0	5.3	9.1	Recovering from relapse
	74	10.9	4.9	6.9	Recovering from relapse
5	147	14.7	4.3	6.4	In remission
Controls†		23±6	2.8±0.7	4.6±1.3	

\* Hypertonic solution placed in bowel.

† Series of 29 persons from studies by Lee, Code, and Scholer (7) and by Reitemeier, Code, and Orvis (8); values following the ± sign are the standard deviations of the means.

TABLE II

*Group 2—Rate of absorption of water from small bowel of patients with sprue*

Case	Test	Initial rate, % absorbed per minute	Minutes required for absorption of		Clinical status
			50%	67%	
6	234	6.4	7.5	13.1	Relapse
7	271	7.1	6.9	10.8	Relapse
9	274	9.4	5.5	9.2	Relapse
10	259	10.4	5.3	10.4	Remission
11	198	20.0	3.1	4.0	Recovering from relapse
12	236	21.7	2.3	3.1	Recovering from relapse
13	254	25.0	2.7	3.4	Remission
14	262	26.3	1.9	2.6	Remission

these earlier studies; the mean initial rate of water absorption, per minute, was 23 per cent of the administered water (standard error of mean 1.1); the slowest rate was 14.8 per cent per minute. All of the patients with sprue who were in relapse had rates that were slower than this (Table I). In general, the rate of water absorption paralleled the clinical condition of the patient, the slowest rates of absorption being encountered in patients in relapse and the most rapid rates in those recovering or in remission. This generalization was also reflected in the time required for absorption of 50 per cent and 67 per cent of the administered water.

*Patients in whom rates of absorption of both water and sodium were tested simultaneously*

In this group of tests the rates of disappearance of water and sodium from arterial blood were determined individually for each patient, thereby eliminating the use of a mean disappearance rate in the calculation of the rate of absorption. The initial rates of absorption of water in three healthy persons using this refinement in technic were 16, 21 and 24 per cent per minute, which values are within the ranges of those obtained in normal persons with the less accurate procedure. Once again, in this more accurate series of observations, all of the patients in relapse had rates of absorption of water that were slower than those of normal persons and there was, in general, a parallelism between the rate of absorption of water from the small bowel and the condition of the patient (Table II). The combined results of the two groups of observations allow the general conclusion that the rate of absorption of water from

the small bowel of patients with sprue while in relapse and under fasting conditions is slower than that of healthy persons, but when the patients are in a remission the rate approaches or becomes equal to that of normal persons.

The rate of absorption of sodium from the small bowel of the patients with sprue was even more decisively retarded than was the absorption of water. Tests of the rate of absorption of sodium have been made on 12 healthy persons in the course of other studies (unpublished data). The mean initial rate of absorption from the small bowel of the group was 9.5 per cent per minute and the slowest rate encountered was 6 per cent per minute. Only one of the patients with sprue had a rate of absorption that fell within the normal range, and this patient had a very mild form of the disease and was in remission at the time of the test (case 14, Table III). All of the patients studied during a relapse had exceedingly slow rates of absorption, ranging from 0.6 to 3.8 per cent per minute, and once again there was a rough correlation between the degree of impairment of the absorption of sodium and the clinical condition of the patient.

*Hypomotility*

The 10 gm. of barium sulfate suspended in the labeled water and placed in the small bowel did not allow a very precise estimate of motility of the small bowel but it was sufficient to demonstrate the decisive roentgenographic difference shown previously by others between sprue patients in relapse and healthy persons. In the patients, the barium spread very slowly through the abdomen and often remained "puddled" in the upper part

TABLE III  
Group 2—Rate of absorption of sodium from small bowel of patients with sprue

Case	Test	Initial rate, % absorbed per minute	Minutes required for absorption of		Clinical status
			50%	67%	
6	234	0.6	80.0	112.5	Relapse
7	271	0.7	> 85.0		Relapse
8	188	3.8	21.8	49.7	Relapse
9	274	0.8	> 85.0		Relapse
10	259	0.7	97.0	115.0	Remission
11	198	4.0	15.4	35.5	Recovering from relapse
12	236	2.8	18.7	29.2	Recovering from relapse
13	254	5.7	10.1	14.0	Remission
14	262	10.4	4.6	6.5	Remission
Mean of 12 healthy persons*		9.5	6.3	8.0	

\* Series from study by Reitemeier, Code, and Orvis (8).

of the small bowel throughout most of the test, whereas in healthy persons the same amount of barium suspension was quickly distributed over a wide area.

#### DISCUSSION

It should be emphasized at the outset that intestinal absorption as determined by the technics employed in this study is the unidirectional passage of the labeled material from the lumen of the bowel to the arterial blood. It is not a measure of the net result of exchanges in both directions across the intestinal mucosa which has often been used by others as the index of absorption.

Wollaeger and Scribner (1) found that absorption of water was retarded in patients with sprue when the water was taken during or following a meal. The results obtained in the present study demonstrate that the absorption of water is retarded in patients with sprue even in the absence of food. These results confirm the earlier findings of Taylor (3). They indicate in addition that the degree of retardation parallels in a rough way the condition of the patient, being greatest during exacerbations of the disease. The present study also confirms the findings of Newsholme and French (5) that there is a delay in the absorption of sodium from the small intestine of patients with sprue. The degree of the defect of absorption is greater for sodium than for water. The question arises, "Is sodium the anchor that holds the water in the bowel?" It seems likely that other factors are also involved.

Although this investigation demonstrates slowed absorption of water and sodium from the small bowel of patients with nontropical sprue, it does not define the mechanism of the defect. Reduced motility was certainly present in the small bowel of all of our patients in relapse. It has been shown by others that the absorption of glucose, methionine (13) and vitamin A (14) from the small bowel of human beings is slowed or hastened by decreases or increases in the motor action of the small intestine. Higgins, Code, and Orvis (15) have recently found that the absorption of water and sodium from the upper part of the small bowel is retarded in healthy persons when propulsive motility is reduced or eliminated by the administration of methantheline bromide. It seems likely that the reduced motility of the small bowel of the patients we studied contributed to the slowed absorption of both water and sodium. Other factors, however, were most likely also involved, for the much greater retardation of the absorption of sodium than of water suggests additional and more specific defects such as might occur in the membrane or membranes separating blood from bowel contents.

#### SUMMARY

The rate of absorption of isotopically labeled water and sodium from the small bowel in 14 patients with nontropical sprue was abnormally slow when the patients were tested during relapse of their disease. When the patients were tested during remission, the rates approached or became equal to those of healthy persons.

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