

Gastrointestinal Absorption with Oleic Acid- I^{131} and L-Methionine- S^{35} in Patients with Ulcerative Colitis.* (23186)

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Several studies have been reported pointing to possible impairment of small bowel absorption in patients with ulcerative colitis (1-5). These studies employed the closed intestinal loop technic or tolerance tests, or dealt with percentage loss of nitrogen in the ileal discharge. As to the increased outputs of nitrogen and of amino acids in the feces of patients with ulcerative colitis, (with intact colons), several observers (6-8) suggested that the increase appears attributable to excess exudate and blood from the colon rather than to unabsorbed proteins. Ruffin *et al.* (9) studied 8 patients with ulcerative colitis using an I^{131} labeled fat (glycerol trioleate). They reported that the average values of the blood were well within normal limits in each of the 8 patients, as was also the radioactive fat material in the stool.

In the present study we employed oleic acid- I^{131} and l-methionine- S^{35} as test material for absorption. By use of basic food substances we minimized, or eliminated completely, the digestive influence required with whole food substances. As noted previously (10) our data suggest that patients with ulcerative colitis might have impairment of absorption of oleic acid and methionine, more especially methionine.

Method. All subjects were hospital inpatients, except 2 patients with ulcerative colitis during stage of remission. Control subjects (16 subjects with 17 studies) were free from any gastrointestinal disease. The ulcerative colitis patients (21 patients with 54 studies) were studied during different phases of the disease. In certain instances the same patient was studied during acute and mild phases of their illness and during remission. Six patients were studied with each tracer substance following ileostomy and

colectomy. During active stages of the disease the colitis patients were on standard supportive therapy (low residue, high caloric, high protein diet; antispasmodics or anticholinergic drugs; sedatives; azulfidine; vitamins). Five patients were also on steroid therapy. The ileostomy-colectomy patients as well as those patients studied during the phase of clinical remission received no medication. This report deals with 71 studies in 37 subjects.

Oleic acid- I^{131} was administered in doses between 5 and 18 μ c (usually 5-10) and l-methionine- S^{35} in doses between 18 and 40 μ c (usually 18 to 22) dissolved in alcohol and water, respectively. These compounds were given at an interval of not less than 3 days, with methionine- S^{35} being given first. The test substance was administered orally at approximately 8 a.m. on an empty stomach. The patients were fed a standard breakfast from 2 to 6 hours (usually 4 hours) after administration of test material. Each fecal sample was collected in individual container and in earlier studies quantity of radioactive material was determined in each sample. In later studies, feces for each 24 hour period through 72 hours was pooled and then analyzed for activity. These specimens were diluted with sufficient water, homogenized with a Waring blender so that a roughly constant specific gravity was obtained (sp. gr. 1.005-1.010). After noting the obtained volumes 3 ml aliquot was taken when counting I^{131} activity and 2 ml aliquot when counting S^{35} activity. A standard, equal to the amount given, was set up for each patient and appropriate calculations were made to determine percent of dose in each specimen. Individual percentages were totaled to give the 72-hour figures. I^{131} activity in liquids was determined in a well-type scintillation counter for 3 minutes while S^{35} activity in liquids was determined with a thin-window TGC-2 Geiger tube for 10 minutes, utilizing constant

* This study was done in cooperation with the Isotope Laboratory of the Department of Radiology in charge of Dr. Howard H. Feigelson

TABLE I. 72-Hour Fecal Excretion of I^{131} and S^{35} following Administration of Oleic Acid- I^{131} and Methionine- S^{35} . Control subjects and patients with ulcerative colitis. (% of orally administered dose.) 71 studies.

	I^{131}					S^{35}				
	No. of patients	No. of studies	Avg	Range	t*	p*	No. of patients	No. of studies	Avg	Range
Control subjects	9	9	5.4	4.2- 6.9			8	8	5.6	4.0- 7.0
<i>Ulcerative colitis</i>										
Acute phase	6	8	12.5	7.6-20.3	3.797	<.01	7	9	39.7	23.5-64.9
Mod. activity	4	4	8.5	6.3-10.2	2.43	<.05	7	7	21.8	12.4-27.6
Remission	6	6	7.3	4.7- 9.9	1.89	>.05	7	7	15.0	10.7-20.0
Ileostomy-colectomy	6	7	13.2	5.4-24.5	2.878	<.05	6	6	26.1	17.7-31.4

*"t" is ratio of mean to stand. error; "p" is probability of occurrence of an event. (See also Batson, H. C., *An Introduction to Statistics in the Medical Sciences*. Burgess Publishing Co., 1956.)

geometry.

Results. 1. The data on fecal excretion are summarized in Table I. In the control subjects the fecal fraction of the administered dose was approximately the same for both I^{131} and S^{35} . 2. Fecal excretion of I^{131} was increased during the acute phase of ulcerative colitis as well as during the period of moderate relapse. The differences between these 2 groups of patients and control subjects are statistically significant. However, the difference in results between patients in remission and the control subjects is not statistically significant. 3. Fecal excretion of S^{35} was increased during the acute phase of ulcerative colitis. As the patients improved clinically, the excretion of S^{35} returned toward control values only slowly so that even during the remission stage, average fecal excretion of S^{35} was still more than twice the average control level. The differences in the results between each of the 3 groups of patients and that obtained in the control group are statistically highly significant. 4. In 6 patients following ileostomy and colectomy, radioactivity of I^{131} in ileal fecal excretion fluctuated considerably. The difference in results is statistically significant. However, in studies with S^{35} ileal fecal excretion was consistently increased and the difference is statistically highly significant. Five of the 6 patients were in excellent health, with the ileostomy and colectomy having been performed from 19 to 58 months prior to the isotope studies; the 6th patient was still convalescing from the operation which was performed 3 months previous to the study.

Table II summarizes results obtained in 5 colitis patients, each of whom was studied during different stages of the disease. The 72-hour fecal S^{35} excretions decreased as the patients improved clinically. However, fecal radioactivity values failed to reach, at any time, the values obtained in control subjects. Such a consistent pattern was not observed with I^{131} .

Summary. Following oral administration of oleic acid- I^{131} patients with ulcerative colitis showed increased fecal excretion of I^{131} during the acute phase of the disease, but it returned toward control values as the pa-

TABLE II. I^{131} and S^{35} Outputs in 72-Hour Stools in 5 Patients with Ulcerative Colitis Studied during Different Stages of the Disease with Oleic Acid- I^{131} and Methionine- S^{35} .

Patient	Date of study	Stage of disease	% test dose	
			I^{131}	S^{35}
S.C.	* 1/13/56	Acute	7.6	39.9
	* 3/ 6	Convalesc.	9.6	17.6
	4/15	Remission		13.7
	*11/29	Acute	13.0	64.9
	* 2/26/57	Ileost.-colec.	12.1	17.7
C.P.	* 9/16/56	Mod. activity	6.3	23.6
	*12/ 1	Remission	9.9	12.5
H.J.	* 6/21	Acute	7.8	29.6
	*12/ 1	Remission	5.1	20.0
P.K.	3/12	Acute	20.3	
	7/ 1	"		57.1
J.L.	* 1/29/57	Remission	8.8	13.6
	11/ 2/56	Acute		51.6
	1/31/57	Remission		17.6
	3/ 1	"	10.9	

* In these patients the methionine- S^{35} study was begun on the specified date and the 72-hr study with oleic acid- I^{131} was begun 4 days later.

tients improved clinically. Following administration of methionine- S^{35} , fecal excretion of S^{35} increased during the acute phase of the disease to a greater degree than the excretion of I^{131} . Also, as the patients improved clinically excretion in the feces returned toward control values only slowly, with the result that during the remission stage of the disease

excretion of S^{35} was still elevated and it was elevated in all ulcerative colitis patients studied to date including those with ileostomy and colectomy.

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Multiplication of Eastern Equine Encephalitis Virus in Mosquitoes Following Intrathoracic Inoculation.* (23187)

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Infection of mosquitoes with arthropod-borne encephalitis viruses by intrathoracic inoculation has been demonstrated(1,2).† Because minimal concentrations of viruses are sufficient to infect mosquitoes by this route, this method appears to be excellent for studying rates of virus development within mosquitoes, uncomplicated by chemical or physical

barriers to infection encountered in the digestive tract.

In the present study the intrathoracic inoculation technic was used to determine rate of multiplication of eastern equine encephalitis (EEE) virus in *Aedes triseriatus* mosquitoes.

Methods. The mosquitoes used were *Aedes triseriatus* 3 to 6 days old. They were anesthetized by 15 to 20 seconds' exposure to carbon dioxide gas immediately prior to inoculation. Method of inoculation was similar

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† L. Whitman, personal communication.