

Cholestyramine and medium-chain triglyceride in prolonged management of patients subjected to ileal resection or bypass

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Summary: The pathophysiology of cholerrheic enteropathy is described and a series of patients reviewed. Of 11 patients with chronic disabling diarrhea and steatorrhea after ileal resection or bypass, two had recurrent ileitis, three had lactose intolerance and six of those operated on five years or more previously had vitamin B₁₂ deficiency. Cholestyramine was given alone or with medium-chain triglyceride (MCT) or Portagen (MCT and lactose). The maximal response occurred when cholestyramine was given with Portagen — significantly reduced stool frequency and weight in all patients and stool fat in five. Restudy of five patients four to 11 months later showed the same pattern of response: cholestyramine with 70% MCT abolished symptoms in four patients (ileectomy) and 100% MCT alone greatly improved the condition of the fifth (extensive small bowel resection).

Résumé: La colestyramine et les triglycérides à chaîne moyenne, adjuvants du traitement chronique de malades ayant subi une résection iléale ou un pontage de l'iléum

L'article rappelle la physiopathologie de l'entéropathie d'origine cholérique et passe en revue une série de malades. Sur 11 malades présentant une diarrhée chronique invalidante et une stéatorrhée consécutive à une résection iléale ou à un pontage, deux souffraient d'iléite récidivante, trois d'intolérance au lactose et les six qui avaient été opérés cinq ans auparavant avaient une déficience en vitamine B₁₂. On a administré la colestyramine, soit seule, soit associée à un triglycéride à chaîne moyenne (TCM), soit au Portagen (TCM plus lactose). La réaction maximale a été obtenue avec l'association de colestyramine et de Portagen: elle a permis de réduire notablement la fréquence et le poids des selles de tous les malades et de réduire les lipides des fèces chez cinq malades. Un examen de contrôle chez cinq malades, dans un délai variant de quatre à 11 mois, a mis en lumière des résultats similaires: la colestyramine avec 70% de TCM a supprimé les symptômes chez quatre malades (iléectomie) et le TCM seul (100%) a permis d'améliorer considérablement le cinquième malade (résection iléale étendue).

A specific syndrome develops after ileal resection or bypass in man.¹⁻³ This consists of watery, sometimes explosive diarrhea, accompanied in many cases by steatorrhea and its sequelae — deficiencies of the fat-soluble vitamins and of vitamin B₁₂. This occurs because active sites for absorption of bile acids^{4, 5} and vitamin B₁₂ have been removed.⁶ When bile acids are no longer absorbed in the terminal ileum increased amounts pass into the colon;⁷ there they interfere with sodium and water reabsorption, resulting in salt loss and watery diarrhea.⁸ Cholestyramine binds the bile acids in the upper small bowel thereby preventing watery diarrhea;² however it may reduce the concentration of conjugated bile acid in the upper small bowel below the critical micellar concentration (CMC), causing or aggravating steatorrhea.

We attempted to minimize this problem by substituting Portagen* for part of the dietary fat. However the lactose component precipitated symptoms of lactose intolerance in some patients; thereafter pure medium-chain triglyceride (MCT) was used. During restudy of five of these patients four to 11 months later we increased the MCT to 70% of the daily dietary fat intake to further reduce steatorrhea.

Patients

Four male and seven female patients aged 14 to 60 years were studied over a one-year period in the metabolic ward of the Victoria General Hospital. Diagnoses and operative procedures and their complications are listed in Table I. Diarrhea and steatorrhea developed after ileal resection in 10 patients and after bypass in one (GD). The length of ileum resected was less than 65 cm. in nine cases; trauma necessitated removal of all of the small intestine except the proximal 90 cm. of jejunum in one (HC). Operation was undertaken for relief of Crohn's disease in eight patients, two of whom had active ileitis when the studies began; when ileitis recurred in one (CG) studies were repeated. GD had been admitted to

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Preliminary reports were presented at the Annual Meetings of the Royal College of Physicians and Surgeons of Canada, January 1969, and the American College of Physicians, April 1969.

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*Mead Johnson Canada, Belleville, Ontario. This preparation contains 38% medium-chain triglyceride, 16% protein and 44% carbohydrate, half of which is lactose.

hospital several times because of hypokalemia (serum potassium <3 mEq./l.) requiring intravenous replacement therapy. HM had had an ileal bladder constructed in consequence of a congenital meningomyelocele and hydrocephalus; she was paraplegic and was being treated for epilepsy with diphenylhydantoin sodium (Dilantin). Severe constipation, relieved by maternal digital evacuation, had been a lifelong problem until a segment of gangrenous ileum caused intestinal obstruction and necessitated ileal resection, after which troublesome diarrhea developed. MC and CF had renal stones removed some time after ileectomy but the composition of the stones is not known.

Methods

The following investigations were carried out in all patients. Roentgenographic studies included upper gastrointestinal series with follow-through and barium enema. Peroral small bowel biopsy was performed at the level of the ligament of Treitz and interpreted according to the criteria established by Rubin and Dobbins.⁹ Lactose tolerance was tested.¹⁰ The patients were examined for neurological deficits secondary to vitamin B₁₂ deficiency. Hematologic and biochemical parameters likely to be affected by malabsorption were determined including prothrombin time and serum and urinary D-xylose values,¹¹ and the Schilling test¹² was performed before and after the administration of intrinsic factor. In six cases (serum iron saturation <20%) bone-marrow aspirates were examined to determine iron stores. For three

days one stool per day was examined for ova and parasites and cultured for pathogenic bacteria. The fat content of 72-hour stool collections was determined by the method of Vogel and Zieve.¹³ Experiments in our laboratories in which we added MCT oil directly to stools showed that 93 to 100% of the MCT is recoverable by this method.

The criteria for active ileitis were abdominal pain and tenderness, fever, leukocytosis, raised erythrocyte sedimentation rate, both white and red blood cells in the stool and roentgenographic evidence of ileal mucosal involvement.

During three three-day periods the number of stools and their weight and fat content were recorded. *Period 1 (control)*: The patients were given a 2000 calorie diet containing 50 g. of long-chain triglyceride (LCT) daily. *Period 2*: Cholestyramine, 4 g. t.i.d. was added. *Period 3*: Portagen, 23 g. was given in place of 20 g. of fat and cholestyramine was continued. One patient (MC) was studied further to elucidate the cause of his continuing steatorrhea.

During restudy of five patients four to 11 months later the proportion of MCT (mainly MCT oil, Mead Johnson) was increased to substitute for 70% of dietary fat, which is all LCT, to provide a palatable diet that would reduce the cholestyramine-induced steatorrhea. A search was made for recurrence of ileitis in patients with Crohn's disease, for sequelae (including renal stones) of the secondary syndrome and for side-effects of cholestyramine. Findings were analyzed by Friedman's two-way analysis of variance by ranks,¹⁴ to avoid having to assume normal

Table I
Complications of ileal resection or bypass

Patient		Diagnosis and operative procedures*	Diarrhea and steatorrhea	Recurrent ileitis	Folate or vitamin-B ₁₂ deficiency	Lactose intolerance	Renal calculi
Age (yr)	Sex						
DP	51 F	Hysterectomy; adhesions; partial colectomy (7cm.) and ileectomy (50cm.)	+				
HM	14 F	Meningomyelocele; ileal bladder constructed; adhesions; ileectomy [†]	+		+		
SA	18 F	Regional ileitis; partial colectomy and ileectomy [†]	+				
HC	32 M	Post-trauma intestinal resection (only 90 cm. jejunum remaining)	+		+		
MD	60 M	Regional ileitis; partial colectomy (25 cm.) and ileectomy (50 cm.)	+				
MC	37 M	Regional ileitis; ileectomy X 2 (total, 54 cm.); nephrolithotomy	+		+		+
CG : 1st admission	55 F	Regional enteritis; partial colectomy, (7 cm.) and ileectomy (64 cm.)	+		+		
CG: 2nd admission	56		+	+			
CF	27 M	Regional enteritis; ileectomy X 3 (total, 57 cm.); cystolithotomy	+	+			+
AP	26 F	Regional ileitis; ileectomy [†] at age 13	+	+			+
GD	39 F	Regional ileitis; ileo-transverse colostomy	+		+		+
SH	55 F	Regional enteritis; partial colectomy (15 cm.) and ileectomy (60 cm.)	+		+		+

*Measurements of intestine are of partly fixed specimens received at Pathology Department.

[†]Approximately 60 cm. of ileum removed or bypassed; exact length not known.

[‡]Studied twice, before and during recurrence of ileitis.

distribution for the observations on each patient.

Results

Three patients had recurrent ileitis and one of these, as well as another two, had lactose intolerance.

Six patients had folate or vitamin B₁₂ deficiency with at least two of three abnormalities in the peripheral blood smear (Table II); five had reduced absorption of vitamin B₁₂, not corrected by the addition of intrinsic factor. (Serum B₁₂ levels were subnormal in three and at the lower limit of the normal range in two.) The sixth (HM), who was being treated with diphenylhydantoin sodium, had low-normal absorption of vitamin B₁₂ (but normal serum levels) and low serum folate values.

Signs of subacute combined degeneration of the spinal cord were detected in HC, GD and SH, but neither the impaired position and vibration sense nor the pyramidal tract involvement had given rise to complaints. These patients had the lowest serum levels of vitamin B₁₂ in the study and had undergone surgery at least five years previously. Four of the seven patients at risk (ileal resection more than five years previously) had had Schilling tests in the year before study, receiving 1000 mg. vitamin B₁₂ intramuscularly as the 'flushing' dose.

In six patients low serum iron values combined with relatively high total iron-binding capacity had resulted in <20% saturation although there was no evidence of iron deficiency in peripheral blood smears; in four however the stainable iron in the marrow was greatly reduced or absent. Three had active ileitis, one had an active duodenal ulcer and one was a woman still having regular menses; no possible source of blood loss was found in the sixth, a male.

The D-xylose test revealed low five-hour urinary excretion in four patients. All had reduced urine volume but in three the serum D-xylose value indicated normal absorption. Serum D-xylose was not determined in the fourth (GD), who excreted 90 ml. of urine in the five-hour test period.

No ova or parasites were seen in the stools. Biopsy specimens of small bowel mucosa were histologically normal. Prothrombin time and levels of serum calcium, phosphorus, magnesium, electrolytes, iron, cholesterol and albumin, and plasma carotene were normal in all patients during the initial study and were not significantly changed in the five restudied after four to 11 months of cholestyramine therapy.

Table II

Findings in parameters likely to be affected by ileal malabsorption
(Underlined figures are values obtained at follow-up after 4 - 11 months)

	Normal values in our laboratories	Diarrhea and steatorrhea only						Ileitis		Lactose intolerance		
		DP	HM	SA	HC*	MD	MC	CG†	CF	AP	GD	SH
		Years since operation						2	13	5	5	
Clinical signs of subacute combined degeneration of spinal cord		0	0	0	+	0	0	0	0	0	+	+
Abnormalities in peripheral-blood smears‡		0	+	0	+	0	+	+	0	0	+	+
Hemoglobin	M, 14-16 g/100 ml. F, 12-14 g/100 ml.	14	13 <u>13.6</u>	13 <u>13.4</u>	12 <u>13</u>	13	14	12 <u>15</u>	7	12	13	12 <u>13.4</u>
Serum iron	65-200 µg/100 ml.	175	182 <u>118</u>	117 <u>93</u>	117 <u>121</u>	57	114	66 <u>71</u>	32	42	69	59 <u>59</u>
Total iron-binding capacity	260-430 µg/100 ml.	300	378 <u>399</u>	270 <u>444</u>	269 <u>270</u>	363	408	477 <u>363</u>	501	417	371	372 <u>330</u>
Iron saturation index	>20%	58	49 <u>30</u>	43 <u>21</u>	43 <u>45</u>	16	28	15 <u>19</u>	6.5	10	19	16 <u>18</u>
Serum folate	>3 ng/ml.	4.4	1.0	5.6	3.1	3.5	4.8	2.7	7.4	2.5	6.1	2.5
Serum vitamin B ₁₂	>200 pg/ml.	---	650 <u>1140</u>	260 <u>400</u>	85 <u>425</u>	475	240	270 <u>410</u>	465	290	175	80
Schilling test	>8% dose excreted in urine/24 hr	7.2	8.7	4.8	0.1	4.5	7.4	4.8	7.4	6.0	2.1	5.1
Prothrombin time	control: 11 sec.	10.5	10.5 <u>11.0</u>	11.5 <u>11.0</u>	10.5 <u>11.0</u>	9.0	9.5	9.5 <u>11.0</u>	10.0	11.0	10.5	10.0 <u>10.0</u>
Plasma carotene§	36-183 µg/ml.	100	53 <u>68</u>	50 <u>59</u>	n.d.‡ <u>n.d.‡</u>	88	134	12 <u>25</u>	27	70	38	85 <u>26</u>
Serum cholesterol	150-300 mg/100 ml.	190	175 <u>160</u>	142 <u>180</u>	62 <u>70</u>	268	267	188 <u>154</u>	132	156	200	235 <u>234</u>
Total serum lipids	500-800 mg/100 ml.	816	528	519	221	1007	---	631	453	514	687	796
Phospholipids	200-250 mg/100 ml.	320	210	185	85	297	---	227	180	208	255	295
Triglycerides	32-245 mg/100 ml.	258	143	192	74	442	---	232	141	150	232	267
Serum calcium	8.5-10.5 mg/100 ml.	9.9	10.1 <u>10.1</u>	9.8 <u>9.9</u>	8.0 <u>9.6</u>	9.6	10.3	9.5 <u>8.9</u>	9.8	9.3	9.8	9.8 <u>10.0</u>
Serum albumin	3.5-5.0 mg/100 ml.	4.6	4.9 <u>4.5</u>	4.1 <u>4.4</u>	4.0 <u>3.3</u>	3.4	5.2	5.1 <u>4.0</u>	4.2	3.7	5.2	4.3 <u>4.3</u>
Serum D-xylose	>25 mg/100 ml. at 1 hr.	78	---	52	32	33	46	---	---	25	---	64
Urinary D-xylose	>25% of dose excreted by 5 hr	25.6	25.9	33.6	6.0	9.1	26.8	31.9	38.7	6.9	7.6	27.3

* HC did not take medication regularly. His serum calcium value later fell to 6 mg/100 ml. on two occasions, at which time he required emergency treatment of the hypocalcemia.

† See footnote to Table I.

‡ At least two of the following: gross variation in erythrocyte size, oval macrocytes, and hypersegmented polymorphonuclear leukocytes.

§ n.d., not detectable

First study (Table III)

Diarrhea and steatorrhea only: In these seven patients, including HC who had had >100 cm. of ileum removed, the addition of cholestyramine to the diet reduced or abolished the diarrhea; stools became formed or semi-formed, abdominal cramps and tenesmus ceased and the average number and weight of stools decreased. Stool fat content increased in four patients and remained constant in three. Substitution of Portagen for part of the dietary fat further reduced the number of stools ($P < 0.001$) and their weight ($P = 0.0036$) and reduced (not significantly) fat content in all but MC. MC was studied further. During three days on a diet containing 46 g. Portagen per day and no cholestyramine he passed seven stools totalling 1475 g. and containing 54.1 g. fat; and while receiving 12 g. cholestyramine along with 46 g. Portagen per day for three days he passed seven stools totalling 1526 g. and containing 42.0 g. fat. We could find no cause for the greater excretion of stool fat when Portagen was given; lactose tolerance was normal.

Active ileitis (two patients): When cholestyramine was given the stool frequency decreased and stool fat increased in both; stool weight increased in one and decreased in the other. When both Portagen and cholestyramine were given stool weight fell while frequency remained the same; fat content decreased in one but increased in the one (AP) who also had lactose intolerance.

Lactose intolerance (three patients): AP (who had active ileitis), GD and SH demonstrated lactose intolerance during testing. When cholestyramine was added to their basic diet the number and weight of stools decreased in all three and the fat content increased in two and decreased in one (GD); when the lactose-containing Portagen was substituted the mean steatorrhea increased two-fold but mean stool weight and frequency were not significantly altered. Further study of GD while on a strict lactose-free diet showed reduction in stool frequency, weight and fat after cholestyramine alone, similar to the results in the seven patients without active ileitis or lactose intolerance. After addition of Portagen all three

parameters increased, reflecting the lactose content of this preparation.

Restudy four to 11 months later (Table IV)

Portagen was omitted from the diet of the patient (SH) with lactose intolerance and the percentage of MCT was increased for all five. The administration of 70% MCT without cholestyramine caused an overall tendency to increased stool weight and fat content and decreased frequency; the addition of cholestyramine reduced stool frequency in three patients, and stool weight and fat content in four. Cholestyramine without MCT decreased stool frequency in three, and both stool weight and fat in two. In the four patients who had had <100 cm. of ileum removed stool frequency, weight and fat content were markedly less ($P < 0.027$) during treatment with 70%

TABLE IV
Stool data during restudy of five patients

Patient	Therapy during 72-hr. study periods (per 24 hr.)	Stools (per 24 hr.)		
		No.	Weight (g.)	Fat excreted (g.)
SA	1. 50 g. LCT (dietary fat)	5	435	10.4
	2. 50 g. LCT; 12 g. cholestyramine	2	102	5.7
	3. 30 g. LCT; 70 g. MCT	4	452	16.4
	4. 30 g. LCT; 70 g. MCT; 12 g. cholestyramine	2	173	8.1
CG ^a	1. 50 g. LCT	5	380	6.9
	2. 50 g. LCT; 12 g. cholestyramine	3	412	10.7
	3. 30 g. LCT; 23 g. Portagen	4	384	9.0
	4. 30 g. LCT; 46 g. Portagen; 12 g. cholestyramine	2	161	4.0
HM	1. 100 g. LCT	2	228	15.5
	2. 100 g. LCT; 12 g. cholestyramine	1/3	21	3.0
	3. 30 g. LCT; 70 g. MCT	1/3	16	7.6
	4. 30 g. LCT; 70 g. MCT; 12 g. cholestyramine	1/3	9	1.4
HC	1. 100 g. LCT	1	697	57.3
	2. 100 g. LCT; 12 g. cholestyramine	2	816	77.0
	3. 30 g. LCT; 70 g. MCT	2	764	63.0
	4. 30 g. LCT; 70 g. MCT; 12 g. cholestyramine	2	724	53.0
	5. 30 g. LCT; 70 g. MCT; 12 g. cholestyramine; sodium bicarbonate; propantheline bromide	2	674	54.3
	6. 100 g. MCT	1	668	35.1
SH	1. 50 g. LCT	2	587	12.7
	2. 30 g. LCT; 70 g. MCT	2	461	8.3
	3A. 30 g. LCT; 70 g. MCT; 12 g. cholestyramine	1	163	12.0
	3B. Same as 3A.	1	115	10.6

^aCG now had active ileitis.

TABLE III
Stool analyses during the first studies

Therapy ^a	Diarrhea and steatorrhea only							Mean	\bar{p} [§]	Ileitis			Lactose intolerance					
	DP	HM [†]	SA	HC [‡]	MD	MC	CG			CF	AP	Mean	\bar{p} [§]	AP	GD	SH	Mean	\bar{p} [§]
Number of Stools per day:																		
1. Control	2	3	4	3	2	6	12	4.6		4	7	5.5		7	7	3	5.7	
2. Cholestyramine	1	2	2	2	2	2	5	2.3	0.027	2	5	3.5	<0.028	5	2	1	2.7	<0.028
3. Cholestyramine and Portagen	1/3	1/3	2	1	1	2	2	1.2	0.001	2	5	3.5	<0.028	5	1/3	1	2.0	<0.028
Stool Weight per day:																		
1. Control	201	95	467	1594	480	650	487	568		905	797	851		797	1992	518	1102	
2. Cholestyramine	122	59	218	922	638	212	585	394	0.027	974	481	727	<0.028	481	243	178	301	<0.028
3. Cholestyramine and Portagen	9.7	9	164	382	404	323	263	222	0.004	609	428	518	<0.028	428	288	229	315	<0.028
Stool Fat Content (g. excreted per day):																		
1. Control	7.5	4.6	7.2	61.1 [†]	12.4	10.4	10.0	16.2		21.9	8.3	15.1		8.3	12.8	6.7	9.3	
2. Cholestyramine	6.0	4.2	9.4	36.6	23.2	11.4	24.7	16.5	0.98	34.7	10.0	22.3	<0.028	10.0	3.7	7.6	7.1	<0.028
3. Cholestyramine and Portagen	0.8	0.1	8.3	33.9	22.6	15.3	6.5	12.5	0.305	31.3	12.2	21.8	<0.028	12.2	12.3	21.2	15.2	<0.028

^aPeriod 1: 2000-calorie diet containing 50 g. of fat (LCT) daily.
[†]Period 2: Same diet, with addition of 4 g. cholestyramine t.i.d.
[‡]Period 3: Same as in period 2, with 23 g. Portagen substituted for 20 g. fat. (Portagen contains 22% lactose.)

[†]At this time HM did not have steatorrhea (<6 g. stool fat per day).

[‡]HC ingested 100 g. fat daily during this 3-day period.

[§]With the method used, ¹⁴ \bar{p} values of the same significance are obtained when including or excluding data for HC (the only patient who had had > 100 cm. of ileum removed).

^{||}AP had both active ileitis and lactose intolerance; therefore, values are listed for both groups for determination of both averages.

MCT plus cholestyramine than when only LCT was given. One patient (HM) became severely constipated when given 12 g. of cholestyramine daily.

CG now had active ileitis. Cholestyramine with normal intake of dietary fat decreased stool frequency but increased stool weight and fat content. When Portagen and cholestyramine were given the values of all three parameters were halved.

We investigated the gastric acid output of HC who had undergone extensive small bowel resection. Basal acid output was 4.4 mEq./hr., rising to 29.73 mEq./hr. (high normal) after maximal histamine stimulation (0.04 mg./kg. body weight). He was treated with sodium bicarbonate and propantheline bromide (Pro-Banthine) to determine whether his level of gastric secretion was contributing to the steatorrhea. This resulted in a tendency to reduced stool frequency and weight but had no effect on fat content. Finally, when 100% MCT alone was substituted for dietary fat, stool frequency decreased to one daily, weight to 668 g. and fat content to 35.1 g.

Follow-up

When discharged from hospital after the first study each patient was told to adjust the dose of cholestyramine until stools were as normal as possible. The daily dose varied from 4 g. (HM) to 12 g.; one patient (DG) took 36 g. daily in an unsuccessful attempt to control an episode of diarrhea associated with an intercurrent illness. Since completion of the study ileitis has recurred in three more patients with Crohn's disease, necessitating further ileal resection in one (SH), but there have been no further persistent changes in biochemical parameters. Several patients have found themselves without a supply of cholestyramine: the profuse diarrhea returns immediately but remits within two days when cholestyramine is restarted.

Discussion

Increased fecal excretion of bile acids^{7, 15} necessitates increased hepatic synthesis of primary bile acids from cholesterol.¹⁶ The CMC of conjugated bile acids, estimated to be 1 to 2 mM,¹⁷ is the minimum necessary to handle normal dietary fat intake. As long as the increased bile-acid synthesis keeps pace with increased bile-acid excretion this intraluminal concentration is maintained, resulting in compensated ileal disorder; there is diarrhea but steatorrhea is minimal or absent. If however the liver cannot synthesize enough bile acid to maintain the total bile-acid pool and keep the jejunal concentration above the CMC the ileal disorder is uncompensated and both steatorrhea^{18, 19} and profuse watery diarrhea occur. Successful interruption of the enterohepatic circulation with the sequestrant cholestyramine abolishes the diarrhea but may cause steatorrhea or increase that already present by reducing the jejunal intraluminal concentration of conjugated bile acids below the CMC.

Cholestyramine is a nonabsorbable quaternary ammonium anion exchange resin with a strong affinity for bile acids.²⁰ When administered as the chloride salt it exchanges the chloride for bile-acid anions (e.g. glycocholate, taurocholate) and binds the bile acids irreversibly in the upper small bowel thereby preventing the deleterious colonic action of the bile acids. Hofmann and Poley³ stated that the diarrhea which develops after ileal resection responds well to cholestyramine provided <100 cm. has been resected and <20 g. fat is being excreted daily in

the feces. This was not the case in all of our patients: the cholestyramine-induced response was identical in HC (only 90 cm. of jejunum remaining), in nine patients who had had <100 cm. of terminal ileum removed and in CF who had active ileitis and was excreting >20 g. fat per day. Furthermore CF and the other two patients with active ileitis and steatorrhea (<100 cm. ileum removed) had decreased stool frequency but increased fat (stool weight was increased in two but decreased in AP) while taking cholestyramine only, and unchanged frequency and significantly decreased stool weight when MCT was added (fat was decreased in two but increased in AP).

MCT is a synthetic oil usually made by fractionating coconut oil.²¹ The carbon chain of its fatty acid comprises mainly caprylic acid (eight atoms) and capric acid (10 atoms). MCT has unique properties: it requires neither emulsification before splitting by pancreatic lipase nor micelle formation before absorption because it has greater water solubility than LCT, the usual fat in food. LCT however, whose fatty-acid carbon chain comprises 14 to 20 atoms, requires emulsification, pancreatic lipase activity and micelle formation before absorption. Whereas LCT is resynthesized and transported as chylomicrons in lymph, MCT is absorbed directly into the portal blood stream; even when the concentration of conjugated bile acids is below the CMC (e.g. after ileal resection or bypass¹⁸), MCT is absorbed effectively, caloric intake is maintained and steatorrhea is reduced.

Portagen (which contains MCT and lactose) precipitated lactose intolerance in three of our patients. When they were fed a lactose-free diet cholestyramine dramatically reduced the diarrhea and steatorrhea — a response similar to that in the seven patients without lactose intolerance or recurrent ileitis (Table III). The cholestyramine-Portagen combination did not produce such a clear-cut response in the patients with active ileitis; in fact this failure alerted us subsequently to the possibility of lactose intolerance or active ileitis. One subject (MC) who did not have lactose intolerance excreted more fat when Portagen was substituted for part of the dietary fat, a result perhaps of competition between MCT and LCT for absorption when MCT is added to the diet.²²

The substitution of lactose-free MCT for part of the dietary fat provided a palatable diet which, when administered with cholestyramine, reduced stool frequency, weight and fat content. In most cases the watery feces were replaced by one or two semiformal or formed stools per day. One patient no longer requires periodic admission to hospital for treatment of very severe diarrhea accompanied by hypokalemia. Another, whose diarrhea was disabling, had spent her postilectomy years confined to home or in the local psychiatric hospital; this situation was abolished by cholestyramine therapy and she no longer requires tranquilizers.

Renal stones containing calcium oxalate may develop in patients who have undergone ileal resection when the proportion of glycine-conjugated bile acids is increased,¹⁹ with subsequent glyoxalate formation and increased urinary excretion of oxalate. Renal stones of unknown composition had been removed from two patients in the study. Cholesterol gall stones are reported to be more common in patients who have undergone ileal resection;²³ no patient in this study had symptoms indicating this disorder and no gall stones were visible on plain roentgenograms. Cholecystography was not performed.

When these patients were first seen some had neurologic and hematologic evidence of vitamin B₁₂ deficiency and there was a high incidence of incipient iron deficiency. One patient had low serum folate values, probably a result of anticonvulsant therapy.²⁴ All these deficiencies responded to standard replacement therapy. Management with cholestyramine, the judicious use of MCT, exclusion of lactose from the diet and vigorous replacement therapy with hematinics abolished the diarrhea and related symptoms. The residual steatorrhea is acceptable and general health is greatly improved.

The authors thank Dr. Malcolm A. MacAulay, Director of the Department of Clinical Chemistry, Nova Scotia Institute of Pathology, for stool analyses; Mrs. Mary Chipman, Department of Preventive Medicine, Dalhousie University, for statistical evaluation; and Miss Ursula Matthews, Editorial Service to the Faculty of Medicine, for her invaluable help in preparing this manuscript.

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