(or its reciprocal conductance) in response to intravenous norepinephrine. There is first a decrease in femoral vascular resistance; this is then followed by an increase in resistance, believed due to the vasoconstrictor action of the drug on the femoral vessels. Brown and Remington(7) attribute the initial fall in resistance to passive distention of the vessels as a result of the rise in central arterial pressure. We suggest that an additional factor may be baroreceptor reflexes activated by the rise in pressure, and operating to produce reflex vasodilation. We have, in this investigation, avoided intravenous injections in favor of intra-arterial injections of doses estimated beforehand to produce little or no systemic pressor effect. Response to intra-arterial injections is monophasic, resistance being increased. Our results suggest that there may be impairment in *pressor* responses of the adrenalectomized animals to *threshold* doses of norepinephrine which is not apparent with higher doses(1). This suggestion is supported by previous findings by Remington and coworkers(8). However, analysis of the responses to threshold stimuli is also subject to greater influence from measurement errors, errors resulting from spontaneous pressure changes, etc.

The lower blood pressure and femoral blood flow values, and the higher femoral resistance values present initially in the adrenalectomized animals are in accordance with the results of Brown and Remington(7) and Wyman, Fulton and Shulman(9).

Summary. Femoral vascular resistance as calculated from pressure/flow ratios was used as an index of vascular responsiveness to norepinephrine in control and adrenalectomized dogs. As indicated by changes produced by small *intra-arterial* doses of norepinephrine, there was no impairment in vascular responses of adrenalectomized animals when compared to controls.

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Absorption of Chimyl Alcohol in Man.* (24783)

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Metabolism of glyceryl ethers has received scant attention, although their distribution in nature is widespread(1,2). Since their discovery in 1922 by Tsujimoto and Toyama, these compounds have been noted as major components of non-saponifiable fraction of many marine oils(3) and are found also in mammalian species, even in human atheromata(4). They are alpha-glyceryl ethers of long-chain fatty alcohols; the ether bond is resistant to alkaline hydrolysis. When the ether linkage is made with oleyl alcohol, the glyceryl ether is called selachyl alcohol; with stearoyl alcohol-batyl alcohol; with palmitoyl alcohol - chimyl alcohol. When the other 2 hydroxyl groups of glycerol are esterified with

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fatty acids, the molecule is called an alkoxydiglyceride(5). The presence of batyl alcohol in bone marrow(6) has stimulated interest recently in its role in hematopoiesis(7-9) and in radiation sickness(10). The possible effectiveness of this compound as an antidote for bracken poisoning in cattle(11) has recently been questioned(12). The present report deals with absorption of labelled chimyl alcohol in man; it follows earlier studies in rats (13). In confirmation of the animal work, the present data show that in man chimyl alcohol is well absorbed, and that in the mucosa a significant cleavage of the ether linkage takes place. The findings are theoretically important, for they indicate the presence in the mucosa of hitherto undefined enzymatic mechanisms.

Materials and methods. Labelled material. [1-C^{14}]-hexadecyl-alpha-glyceryl ether (chimyl alcohol) was prepared from [1-C^{14}]-cetyl alcohol according to procedure of Holmes *et al.*(6). The labelled compound was the same as that used in animal studies(13), and had a specific activity of 1 x 10^5 c.p.m./mg (0.2 μc). All counting was done in infinitely thin layers in aluminum planchets with windowless flow counter; at least 1000 counts were made in all cases. *Patients.* This study was performed on 2 patients. The first (A) was a 52-year-old Puerto Rican woman with chyluria whose clinical history has been described(14). Previous investigations on absorption of various fats by this patient also have been reported(15,16). All studies were made on metabolic ward of Rockefeller Institute Hospital. The second patient, investigated in Depts. of Medicine and Clinical Chemistry, Univ. of Lund, Sweden, was a 67-year-old male with bilateral chylothorax secondary to carcinoma of unknown origin. Although he was in good nutritional state, it was necessary to perform thoracenteses twice a week. The composition of his chyle fat was the same as that of normal human thoracic duct lymph(17), mainly triglyceride with 10% phospholipids and 2-3% cholesterol and cholesterol esters. Paper electrophoresis of serum and chyle showed identical patterns of proteins. When 10% protamine sulfate was added to his chyle, the chylomicrons immediately aggregated and floated to the surface, as described by Brown(18) for rat chyle.

Metabolic design. Patient A was maintained at constant body weight with orally-administered liquid formula(14), essentially "fat-free," fed 5 times a day. On day of this experiment the 7 a.m. portion was enriched with 2.5 g corn oil containing 25 mg (5 μc) of C^{14}-labelled chimyl alcohol. Through rest of day the fat-free formulas were ingested at usual times. The patient was continually ambulatory. Complete urine collections were made in 3-hour periods for 12 hours. Urine was immediately diluted with equal volume of 95% ethanol and stored at 4°C prior to analysis. Patient B was maintained on a mixed hospital diet. On first day of experiment the chest was emptied as completely as possible by thoracentesis, and 2 g olive oil containing 18 mg (3.6 μc) of C^{14}-labelled chimyl alcohol was fed on a piece of bread. A second thoracentesis was performed 48 hours later with removal of 800 ml of chylous fluid. This was diluted immediately with equal volume of 95% ethanol and stored at 4°C until analyzed.

Extraction of lipids from chyle and from chylous urine with 20 volumes of ethanol: ether (3:1). Non-lipids were eliminated by petrol ether (60-70°C) rectification after concentration of the extracts to small volumes under high vacuums at temperatures below 30°C. Aliquots were taken for total counts. *Phospholipids* were precipitated twice with ice-cold acetone and dissolved in petrol ether. After hydrolysis analyses were made of phosphorus, total fatty acids and C^{14}-labelled fatty acids. *Non-esterified fatty acids* were removed from the acetone-soluble lipids by passage over Amberlite IRA-400 and were recovered as described by Borgström(19). The remainder of the extract, after removal of phospholipids and free fatty acids, was applied in benzene to a silicic acid column. *Triglycerides and chimyl alcohol di-esters* were eluted together with benzene; benzene: chloroform (85:15) eluted no labelled material; free *chimyl alcohol* was eluted with chloroform. This chromatographic behavior of the alkoxydiglyceride and of the free alco-

hol has been described(13,20). Hydrolyses were performed with 4% KOH in 95% ethanol with sufficient benzene added to dissolve the lipid. After evaporation, the mixture was acidified and extracted into petrol ether. In the case of hydrolysis of the triglyceride-chimyl alcohol di-ester fraction, fatty acids were removed with alkaline 50% ethanol, leaving non-saponifiable material (including chimyl alcohol) in the petrol ether phase. Fatty acids were recovered and subjected to permanganate oxidation(21). Unoxidized saturated acids were recovered; they contained all radioactivity originally present. These saturated acids were subjected to reversed phase chromatography according to Howard and Martin(22), with titration and counting of the effluent curve. Almost all activity was confined to one titration peak. Radioactive fractions were combined, fatty acid recovered and diluted with unlabelled palmitic acid. Five recrystallizations from 90% aqueous acetone were carried out and changes in specific activity were followed. Labelled chimyl alcohol eluted in chloroform was recovered, diluted with unlabelled chimyl alcohol, and the mixture recrystalized 5 times from petrol ether, assaying specific activity changes at each step. In Patient A *fecal lipids* were extracted with hot 95% ethanol from stools of day 1, 2 and 3. Only a small number of counts were noted (5% of administered dose). Fecal lipids were saponified; all counts remained in the non-saponifiable fraction.

Results. In Patient A the fecal data showed that 95% of administered labelled chimyl alcohol was absorbed. Approximately 40% of the dose was recovered in urine within 12 hours after administration, indicating that the patient shunted about 40% of her intestinal lymph into the urinary tract. This estimate of shunt size agrees well with data presented previously(16), based on measurements of total lipid. Since 40% of administered dietary fat and 40% of administered labelled chimyl alcohol were recovered in urine in approximately the same period, it seems probable that in man all absorbed chimyl alcohol is transported *via* the lymphatic pathway. The same conclusion was reached in experiments on rats(13).

Radioactive products were identified in 1) phospholipid fatty acids, 2) non-esterified fatty acids, 3) chimyl alcohol di-ester (in the chimyl alcohol moiety), 4) free chimyl alcohol, and 5) fatty acids of triglycerides and chimyl alcohol di-esters. In the case of 1) and 5) above, the labelled fatty acid was identified as palmitic acid by chromatographic isolation and by dilution with unlabelled palmitic acid and recrystallization without change in specific activity. By the same means labelled chimyl alcohol was identified in lymph lipids. Proportions of labelled products in these 5 fractions were very similar in the 2 patients (Table I); the results are entirely in agreement with data in rats(13). About 40% of absorbed chimyl alcohol was transported in lymph as free alcohol while about 10% of administered free chimyl alcohol had become esterified. However, 50% of the alcohol had been converted to palmitic acid. This palmitic acid appeared to have entered the general fatty acid pool of the mucosa, for it became esterified with phospholipids and triglycerides in about the same proportions as in man with absorption of fatty acids(15).

Failure to find labelled products in the saponifiable fraction of fecal lipids indicates 1) rupture of ether linkage of chimyl alcohol,

TABLE I. Distribution of Radioactivity in Lymph Lipids after Oral Administration of C^{14}-Labelled Chimyl Alcohol.

Patient	% of admin. activity recovered in lymph lipids	Distribution of radioactivity, % of total recovered				
			Chimyl alcohol		Esterified FA	
		FFA	Free	Esterified	Phospho-lipids	Trigly-cerides*
A (12 hr)	39	.5	42	11	1.5	45
B (48 ")		.3	32	14	1.7	52

* Includes fatty acids esterified with chimyl alcohol.

2) conversion of palmitoyl alcohol moiety to palmitic acid, and 3) re-esterification of palmitic acid into glycerides and phospholipids must have occurred in the intestinal mucosa. However, unpublished experiments in rats by Blomstrand(23) indicate, that chimyl alcohol can be esterified in the intestinal lumen. This reaction is analogous to the breaking and making of glyceride ester bonds which occurs in the intestinal contents of rats(24) and man (25), presumably under the control of lipase.

Summary. Labelled chimyl alcohol fed orally to a patient with chyluria was almost completely absorbed, and 40% of administered activity was recovered in 12 hours in the urinary lipids. About half of radioactivity in lymph was identified as chimyl alcohol, about three-fourths of which was present as free chimyl alcohol, and a fourth had become esterified. The remaining 50% had been converted to palmitic acid, and found in triglycerides, phospholipids and free fatty acids in proportions expected when dietary palmitic acid is transported from the gut. Repetition of this study in a patient with chylothorax gave essentially the same results. The results indicate that rupture of ether linkage of chimyl alcohol can occur in the intestinal mucosa of man, as in the rat, and that the palmitoyl alcohol moiety is readily oxidized to palmitic acid.

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Growth of Human Cancer (H Ep 3) in Normal Rats.* (24784)

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Many workers have attempted to transplant human cancers into experimental animals but only a few have devised successful procedures. Greene(1,2), by inoculating into the anterior chamber of the eye, or into the brain of normal animals found that tumors "in the final developmental stages of meta-

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