are controlled ultimately by the hypothalamus. The results cast no light on the mechanism whereby these alterations in apparent enzyme activity occur(1,9).

The residual response to histidine found in both hypophysectomized animals and those with lesions, is of interest since it stands in contrast to the complete block of response found by Knox in adrenalectomized rats(1). This response in our experiments appears to be similar to augmented activity of the enzyme produced by histidine in cortisone-treated adrenalectomized rats(1). It thus appears that histidine can still produce an elevation in tryptophan peroxidase activity even in the presence of a constant output of cortical steroids whereas no response occurs if steroid output is zero. The role of corticoids in response to histidine, appears to fall into the category of responses which Ingle has called the permissive action of cortical steroids(10). Presumably in our experiments, the residual response to histidine must be brought about either by another regulatory system in the body, such as the sympatho-adrenomedullary system, or by a direct effect of histidine on the liver cell. Because of the multiple agents which can bring about increase in tryptophan peroxidase, this latter possibility appears to be unlikely. Another possible explanation for residual response to histidine would be that degradation of cortical steroids might be decreased under these circumstances, thereby producing a rise in blood level of steroid in the presence of a constant output of steroids as suggested by Steenberg and Ganong(11). The elevated level of steroid could then bring about the enzyme response.

Conclusions. 1. Histidine produces a small decrease in adrenal ascorbic acid concentration in normal rats, but not in rats with hypothalamic lesions interrupting the supra-optico-hypophysial tract. 2. Hypothalamic lesions or hypophysectomy produce a decrease in the response of tryptophan peroxidase to histidine but fail to block the response completely.

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A Screening Test for Malabsorption Syndromes. (24707)

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Progress in understanding of malabsorption syndromes has been hampered by lack of simple methods of diagnosis. The I^{131} labeled fat absorption test has become a valuable tool in diagnosis of these conditions but it does not fulfill all requirements of a simple reliable screening test. Plasma becomes turbid after fatty meal primarily because of increase in neutral fat or triglyceride(1). Osmon, Zinn and Whorton(2) and Turner(3) have shown that plasma lactescence fails to develop after fat ingestion in patients with chronic pancrea-

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titis. Gardner(4) found similar results in patients with tropical sprue. We have measured changes in plasma optical density (O.D.) after fatty meal in 20 normal subjects and in 15 patients with a variety of malabsorptive defects. The data have been compared with measurements of I^{131} fat absorption, serum carotene, d-xylose excretion, and metabolic fat balance determinations.

Material and methods. After 12 hour fast, a homogenized meal containing 50 ml of corn oil, 240 ml of skim milk and 50 μc of I^{131} labeled triolein was given each patient. The meal has 8.2 g of protein, 14.3 g of carbohydrate, and 51.9 g of fat. Twenty drops of Lugol's solution were administered evening before the test to block I^{131} uptake by the thyroid. Eight ml of blood drawn from antecubital vein was put in heparinized tubes. Samples of blood were obtained before ingestion of test meal and every 2 hours thereafter for 10 hours. Plasma O.D. was measured in Coleman Jr. spectrophotometer at wave length of 650 mμ (12 mm light path) against water blank and expressed in optical density units. Radioactivity in 2 ml of plasma from each sample was counted in scintillation type well counter. Plasma volume was estimated from surface area and total plasma radioactivity expressed as percent of amount ingested. Seventy-two hour stool collections were counted individually and stool radioactivity was also expressed as percent of administered isotope. Amount of radioactivity in the stool was measured with gamma counter under conditions which minimize effects of variation in shape and volume of specimens. Counting was continued to give statistical reliability of at least 5%. Serum carotene was estimated by the method of Quaife, Scrimshaw, and Lowry(5), and d-xylose by that of Roe and Rice(6). Standard metabolic fat balances were measured in 5 day periods. Patients were studied for at least 2 periods. Aliquots of diets were pooled, homogenized and analyzed for fat by method similar to that of Fowweather and Anderson(7). A Goldfisch apparatus was used for extraction. Stools were pooled, homogenized and aliquots analyzed for fat. Stool fat was expressed as percent of intake. All chemical determinations were in duplicate.

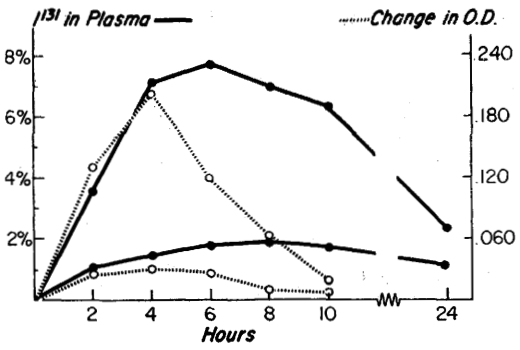

FIG. 1. Upper 2 curves show changes in plasma optical density and radioactivity in normal group, and 2 lower curves show changes in the abnormal group. Each plot represents avg of all determinations at each time interval.

Results. In the control group maximal change in plasma optical density averaged 0.260 ± 0.126 and 0.054 ± 0.052 in the abnormal group. Difference between means is statistically significant, $p<0.001$. Change in plasma optical density and rise in plasma radioactivity are shown in Fig. 1. Difference between peak values for normal and abnormals is significant at 0.1% level. Table I shows relationship between change in plasma O.D., serum carotene, urinary excretion of d-xylose, stool radioiodine, and fat balance studies in the abnormal group. For convenience patients were divided into 3 groups: primary absorptive defects, defects of absorption secondary to surgery of the G.I. tract, and miscellaneous.

In patients with primary absorptive defects the change in O.D. was less than 0.1. In 3 patients there was no change. These data agreed well with all parameters of fat absorption we studied. In patients whose malabsorption was secondary to an operation, plasma O.D. failed to rise to normal values in all but one patient, C.S. Urinary excretion of d-xylose was normal in this patient although stool radioactivity was elevated. Patients in the miscellaneous group, plasma O.D. changes were abnormal in all cases except for a single borderline value in W.B.

Table II has results before and after therapy in 2 patients with sprue and one patient

TABLE I. Comparison of Absorptive Tests in Malabsorption Syndromes in Humans.

	Group	Patient	Diagnosis	Max change O.D.	Serum carotene, μg/100 ml	Urinary d-xylose, g/5 hr	Fat* balance	Stool* radioassay
I	Primary absorptive defects	M.S.	Whipples	0	22	3.5	37.2	59.9
		R.C.	Sprue	.070	21		40.5	20.8
		N.R.	"	0	12	1.4		53.9
		E.C.	"	0	0		68.9	24.9
		C.C.	"	.035	14	1.2	7.0	41.6
							11.0	
II	Secondary to surgery	H.S.	Subtotal gastrectomy	.059	14	4.5	28.5	63.6
		R.V.	*Idem*	.080	43			25.4
		H.M.	"	.025		.7		38.0
		B.G.	Extensive small bowel resection	0	8	1.5	82.1	91.5
		M.C.	*Idem*	.095	69	.9	12.8	46.1
		C.S.	Resection of terminal ileum	.190		6.5		29.9
III	Misc. diseases	R.B.	Fibrocystic disease	.032	20			19.1
		W.B.	Small bowel diverticula	.115	43	5.5	5.5	4.1
				.065			14.7	5.0
		G.S.	Chronic pancreatitis	.014	17			18.7
		N.Y.	*Idem*	.040	8			55.7

* Stool fat expressed as % of quantity ingested.

with chronic pancreatitis. Clinical improvement was accompanied by normal rise in plasma optical density after a fatty meal.

Discussion. The fat tolerance test is a semi-quantitative measure of fat absorption. It is modified by many other factors, such as gastric emptying, rate of lymph flow, fat transport, utilization, and deposition. After ingestion of the standard fat meal all subjects in the control group had a change in plasma optical density of greater than 0.1. Therefore, we have chosen this figure as the lower limit of normal. Only 2 patients with clinical and laboratory evidence of malabsorption had rises in plasma optical density greater than 0.1. One of these, C.S., had had resection of distal portion of ileum for regional enteritis. Clinically he was malnourished and complained of explosive diarrhea, not grossly fatty. Urinary excretion of d-xylose was normal but there was an excessive amount of radioactivity in the 72 hour stool. We noted, however, that various measures of absorption in patients with postsurgery malabsorption do not agree as well as in patients with primary absorptive defects. Similar findings in serum carotene have been reported by others(8). Patient W.B. had a borderline maximal change in plasma optical density of 0.115 on one occasion, although on another the rise was only 0.065. There was similar variation in fat balance studies but stool radioactivity was normal on 2 occasions after ingestion of I^{131} labeled triolein. This patient had mild malabsorption associated with multiple jejunal diverticula. Fluctuations in fat absorption

TABLE II. Tests of Absorption before and after Therapy.

		O.D.	Serum carotene, μg/100 ml	Urinary d-xylose, g/5 hr	Stool* radioassay	Fat* balance
C.C.	Sprue in relapse	.035	14	1.2	41.6	9.0
	After gluten-free diet	.337	121	4.5	6.6	9.4
R.C.	*Idem*	.070	21		20.8	40.5
		.140	79	8.2	9.5	6.1
N.Y.	Chronic pancreatitis	.040	8		55.7	
	with pancreatin	.485			10.7	

* Stool fat expressed as % of quantity ingested.

probably reflect natural variations of the disease. All other patients with clinical and laboratory evidence of malabsorption had a rise in plasma O.D. of less than 0.1.

Summary. Our studies indicate that measurement of changes in plasma optical density after a fatty meal is a simple and reliable screening test for patients with malabsorption syndromes. It is of value in following the course of these diseases and in evaluating response to therapy.

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Effects of Hepatectomy on the Response of the Uterus to Estradiol-17-β.* (24708)

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A peak in uterine fluid imbibition in sexually immature rats is reached within 6 hours following estrogen stimulation. This is followed by a period of cellular proliferation and gradual increase in total uterine weight(1). Hechter *et al.*(5) and Kalman(7) showed that early effects were due to a change in capillary permeability. Roberts and Szego(10-12) found that removal of two-thirds of liver greatly reduced early stimulating effect of estradiol on rat uterus. This led them to study of uterine response to estradiol at various intervals after partial hepatectomy and they observed that sensitivity to estrogen was gradually regained. They correlated restoration of estrogen activity with liver regeneration. In the present study, this relationship has been examined by using a slightly different approach and a different interpretation of data is presented.

Materials and methods. The effect of partial hepatectomy on uterine response to estradiol was studied in sexually immature rats by means of methods developed by Astwood (1). Ten animals were used in all control and experimental groups. Rats (Harvard strain) 24-25 days old and weighing 54 to 60 g were given a single subcutaneous injection of 0.1 μg estradiol 17-β immediately after 60%-70% of the liver was removed. Uteri and livers of different groups were removed at 6, 9, 12, 15, 18, 21, and 30 hours after treatment. The organs were weighed at autopsy and again after oven-drying 24 hours at 90-100°C, the difference reflecting water content. The technic of partial hepatectomy was based on those reported by Higgins and Anderson(6) and Roberts and Szego(10). The mean value and standard error are presented for key groups.

Results. On the basis of fluid imbibition, partial hepatectomy decreases normal response of uterus to estradiol as seen 6 hours after treatment (intact control, 81.8% $\pm$ 0.02%; intact treated, 87.1% $\pm$ 0.3%; hepatectomized control 81.6% $\pm$ 0.4%; hepatectomized treated, 84.2% $\pm$ 0.6%). However, when uteri were removed at various times later than 6 hours, increases in weight clearly indicate that the effect of partial hepatectomy on accumulation of water in the uterus is one of retardation rather than inhibition (Fig. 1,

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