of endogenous ACTH. Alternative explanations have not been excluded, however, such as stimulation by hydrocortisone of insulin secretion from the pancreas. Further suggestive evidence that endogenously secreted pituitary hormones may effect fat mobilization is the well known tendency of hypophysectomized rats to become relatively obese when fed and to resist lipid depletion when fasted despite their proneness to hypoglycemia. Knobil(9) has demonstrated that adipose tissue from hypophysectomized rats releases smaller amounts of fatty acid *in vitro* than that from normal rats, whereas treatment of the hypophysectomized rats with STH restores this defect toward normal. The contributions of increased insulin sensitivity and lowered basal metabolic rate to impaired fat mobilization of such animals are yet to be evaluated.

Summary. Purified corticotropin and growth hormone both stimulate lipid mobilization from the epididymal fat depots of fasting mice. Hydrocortisone failed to induce lipid loss in intact mice and inhibited fat mobilization in adrenalectomized mice, indicating that the lipid mobilizing effect of corticotropin is not mediated by adrenal stimulation. Furthermore, inhibition of fat loss by hydrocortisone in adrenalectomized mice could be overcome by simultaneous administration of corticotropin. The results demonstrate an extra-adrenal action of corticotropin on fat mobilization in the intact animal similar to that induced by growth hormone.

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Mechanism of Inhibition of Gastric Secretion by Fat in the Intestine.* (25217)

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It is well known that gastric secretory activity and gastric motility are inhibited when fat is present in the proximal small bowel(1). This inhibitory effect of fat has been documented by experiments in dogs and humans, and is said to be mediated by an agent circulating in blood(2). The nature of this agent is unknown. Lim *et al.*(3) prepared from mucosa of small and large bowel of dogs a crude extract capable of inhibiting gastric secretion in dogs. They postulated that these extracts and also those prepared later from hog small bowel mucosa contained the hormone "enterogastrone" which under physiologic conditions is released by the small bowel mucosa in the presence of fat. Whereas "enterogastrone" preparations inhibit gastric secretion in dogs and to a lesser degree in humans, they fail to inhibit gastric secretion in the rat(4). Our finding(5) that parenteral administration of bile salts inhibited gastric secretion in rats suggested the possibility of increased resorption of bile salts incident to fat digestion and absorption being the mechanism responsible for gastric inhibition by fat. Our purpose was to determine if rat gastric secretion was inhibited when fat was present in the small intestine and, if so, to what extent this inhibition was affected by presence

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TABLE I. Influence of Presence or Absence of Bile Salts in Lumen of Small Bowel on Inhibition of Gastric Secretion of Pylorus Ligated Rats by Fat in the Intestine.

	No. rats†	Mean % change from paired controls	
		Vol (ml)	Free HCl (meq/l)
Intact rats, 2 ml olive oil*	30	−80% p <.001	−35% p <.001
Bile shunt, " " " *	38	−16% p .1	+ 1%
Bile shunt, " " " + 400 mg Tween 80*	26	−10% p <.2	+ 1%
Bile shunt, " " " + 30 mg ox bile salts*	20	−81% p <.001	−43% p <.001
Bile shunt, 30 mg ox bile salts*	16	−3%	+13%

* Intraduodenal administration.
† Total No. of paired control and treated rats in each group.

or absence of bile from the intestine. Our data show that gastric secretion also in the rat is inhibited by fat. This takes place only when bile constituents, particularly bile salts, as well as fat are present in the small bowel.

Materials and methods. Gastric secretion was measured by pyloric ligation method(6) in 130 rats weighing 160 to 220 g. Prior to pyloric ligation, the rats were fasted for 48 hours in individual cages with wide mesh wire bottoms. During fasting period water was given *ad lib.* Rats were divided into 5 groups of paired control and treated rats. In all rats *except those of Group 1,* the bile duct was shunted to the rectum 24 hours before pyloric ligation, using a technic described previously (5). The entire bile output is diverted from the small intestine and coecum. Pancreatic secretions are left undisturbed. It was established previously that diversion of bile from the small intestine does not alter gastric secretion in the rat. In rats belonging to Group 1 a sham operation was done. Pyloric ligation was performed in all rats under light ether anesthesia. Simultaneously, treated rats received the following intraduodenal injections. Groups 1 and 2: 2 ml of olive oil each. Group 3: 2 ml of olive oil and 400 mg of Tween 80. Group 4: 2 ml of olive oil and 30 mg of ox bile salts. Group 5: 30 mg of ox bile salts in 2 ml of normal saline. Doses were on basis of 200 g of rat weight. They were administered by single injection through a 26 gauge needle inserted into the duodenum immediately distal to pyloric ligature. The paired random controls received the same volume of normal saline. Six hours later the rats were killed and stomachs removed. The gastric content was studied individually for volume and free HCl concentration.

Results. The data are summarized in Table I. Intraduodenal administration of olive oil suppressed gastric secretion in intact rats. Only moderate inhibition of gastric secretion was observed when the same amount of oil was administered to rats of Group 2 in which bile had been diverted from small intestine. This result was not altered by addition of Tween 80 to the oil. However, the same degree of suppression of gastric secretion observed in intact rats occurred when bile salts were added to the oil. Finally, administration of bile salts alone into the duodenum did not alter gastric secretory activity.

Discussion. These data show that the presence of fat in the small intestine decreases gastric secretory activity in rats (as well as in dogs and humans). Following diversion of bile from the small intestine, gastric secretion is not inhibited by fat unless bile salts are added to the administered oil. On the other hand, this same dose of bile salts which had been shown to suppress gastric secretion when administered parenterally, did not alter gastric secretion when given intraduodenally in the absence of fat. It seems unlikely that the relationship of bile salts to gastric inhibition by fat is nonspecific and due merely to their surface active properties in view of the results obtained in Group 3 in which addition of

Tween 80 to the oil did not result in any greater inhibition than observed in Group 2. There is some experimental evidence to suggest that fatty acids are more potent inhibitors of gastric motility than neutral fats(7). Therefore, one could postulate that the lack of inhibition of gastric secretion by olive oil when bile was absent from the small bowel was due to a lower concentration of products of hydrolysis of neutral fat in the intestinal lumen. However, percentage hydrolysis of neutral fat is often normal in spite of absence of bile salts(8). Furthermore, oleic acid, when administered intraduodenally to intact rats, does not have as strong and as consistent inhibitory effects on gastric secretion as olive oil (unpublished data).

Summary. Gastric secretion in the intact rat is inhibited by fat in the small intestine. This inhibitory activity is decreased when bile has been diverted previously from the small intestine. Under these same conditions, addition of bile salts to administered fat results in the same degree of inhibition as in the intact animal.

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Comparative Plasma Levels of Mephenesin, Mephenesin Carbamate and Methocarbamol.* (25218)

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It has been shown in both animal and man, that significantly higher and more persistent plasma levels were obtained by mephenesin carbamate as compared to those of mephenesin(1,2). When a similar pair of related drugs, namely glyceryl quaiacol ether (G.G.E.) and its carbamate, methocarbamol, were compared by several methods, it was found that methocarbamol gave higher plasma levels than G.G.E. Furthermore, methocarbamol gave higher plasma levels than mephenesin or mephenesin carbamate, following oral administration of equimolar amounts of the drugs to dogs(1). Since similar observations in man have not been reported, it was decided to determine the plasma levels of mephenesin, mephenesin carbamate and methocarbamol, following oral administration of equimolar doses of these drugs to humans. Such studies should be of interest because of clinical reports on the prolonged action of methocarbamol in the treatment of painful muscle spasm(3,4,5,6,7).

Materials and methods. Ten healthy subjects, six males and four females, were chosen. Four subjects (Group 1) were started on methocarbamol, three (Group 2) on mephenesin, and three (Group 3) on mephenesin carbamate. About one week later, when the blood was free of these drugs the subjects of the three groups ingested mephenesin or mephenesin carbamate, or methocarbamol in such a manner as to give randomness in the sequence of ingestion of the drugs. The dosage was 4.00 g of methocarbamol; or 3.75 g of mephenesin carbamate; or 3.00 g of mephenesin. These amounts of drugs are equimolar. The total dose was ingested at once—immediately

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