weight. Repeated subcultures of staphylococci and of certain strains of streptococci in the presence of increasing concentrations of either one of these antibiotics result in fairly rapid and marked increases in resistance not only to the antibiotic to which it was exposed but to the other agent as well.

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Role of the Pancreas in Prevention of Fatty Liver in the Hypophysectomized-Thyroidectomized Dog.* (20001)

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The pancreas, by virtue of its exocrine function. exerts a profound influence on the liver. This has been clearly brought out in the case of the fatty liver that appears in the completely depancreatized dog receiving insulin(1). It is shown in this report that the digestive function of the pancreas may be implicated in the development of another type of fatty liver, namely, that observed in the hypophysectomized - thyroidectomized (HT) dog. This type of fatty liver is prevented if choline in the free form is added to the diet (2). Evidence presented here shows that extra methionine is also efficacious. That the fatty liver in the doubly-operated dog is the result of pancreatic insufficiency is indicated by the additional finding that its development can be prevented by feeding raw pancreas.

Experimental. Nine dogs were used in this study. Throughout their stay in the laboratory they were fed, daily, 30 g of lean meat per kg of body weight, in addition to sucrose, vitamins. and a salt mixture. The exact composition of this diet has been described elsewhere(3). The pituitary glands were first removed, and one to 2 weeks later the thyroids were excised. The animals were then divided into 3 groups (Table I). The control dogs (Table I) were fed just the lean meat diet described above. The second group was fed, in addition, 25 g of pancreas with each meal. The third group was fed 2 g of methionine with each meal. To ensure the exact dietary intakes recorded for each dog, forced feeding was resorted to at times. All of the dogs were maintained for not less than 749 days. This period exceeds the minimum time necessary for the consistent development of the fatty liver in HT dogs(2). At the end of the period of observation, livers and blood were removed, and their lipide contents determined by methods previously described(4).

Results. In a preceding paper it was shown that hypophysectomy and thyroidectomy result in the development of a fatty liver in the dog in 217 to 419 days(2). In the present study the livers of the 2 control dogs contained 21.6% and 27.4% total fatty acids (Table I). From 2 to 3% total fatty acids were found in the livers of the dogs fed pan-

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TABLE I. Plasma and Liver Lipides of HT Dogs Fed Pancreas and Methionine.

Dog No.	Body wt, kg: At hypophysectomy	Body wt, kg: At thyroidectomy	Body wt, kg: Final	Period maintained after hypophysectomy-thyroidectomy, days	Supplement fed: Type	Supplement fed: Per meal,* g	Plasma total lipide, mg %	Liver lipides: Wt, g	Liver lipides: Total fatty acids, % wet wt
HT-47	6.5	6.7	8	749	0, control	—	946	290	21.6
49	7	7.6	8.5	749	0, "	—	782	268	27.4
34	7.5	9.4	9.2	826	Pancreas	25	798	260	3
37	6.3	8.7	9.2	826	"	25	1349	278	2.3
48	7	7.2	11.7	750	"	25	945	300	2
50	6.5	6.6	15	750	"	25	2255	405	2
40	8	8.4	10.7	838	Methionine	2	1395	406	2.4
41	6	7.9	8.8	838	"	2	1346	266	1.7
42	8.7	9.6	16.7	838	"	"	1675	652	3.8

* The dogs received 2 meals per day.

creas in addition to the regular meat diet. The livers of dogs fed methionine contained from 2 to 4% total fatty acids.

The values for total plasma lipides are also recorded in Table I. They ranged from 780 to 2260 mg %. The concentration of total lipides in plasma of normal dogs fed the lean meat-sucrose diet does not exceed 750 mg % (5). As in previous studies, all of the HT dogs showed a considerable increase in weight (Table I). This increase was not unexpected because forced feeding was employed to maintain the preoperative caloric intake.

Discussion. The amounts of lean meat fed each HT dog contained approximately 0.5 g of choline and 3 g of methionine, and it is important to recognize that such amounts of lipotropic substances more than suffice to prevent the development of fatty livers in *normal* dogs(1). Our earlier finding, that the addition of a lipotropic substance to the lean meat diet prevents fatty livers in HT dogs, is fully confirmed in the present study with methionine. It was this type of action that led us to suggest that the fatty liver in the HT dog resulted from 1) an interference in the mechanism for release of lipotropic factors from the ingested meat in the intestine and/or 2) defective absorption of these substances. It is well established that the rate of carbohydrate absorption from the intestine is depressed after thyroidectomy(6) and hypophysectomy(7), and it is therefore conceivable that the absorption of free lipotropic substance from the intestinal tract is also depressed. The observation, however, that the feeding of 25 g of raw pancreas per meal is also effective suggests rather that the excision of both thyroid and pituitary glands interferes with the release of lipotropic factors from ingested meat in the intestinal tract. The presence of an intact pancreas in the HT dog is not incompatible with this view since it is reasonable to infer that the exocrine portion of the pancreas, a site of rapid protein synthesis, is functionally depressed by hypophysectomy and thyroidectomy.

Summary. 1. Dogs deprived of both thyroid and pituitary glands develop fatty livers. The livers of 2 such dogs that were fed a diet rich in lean meat for 750 to 840 days contained 22 and 25% fatty acids. 2. The addition of 2 g of methionine to each meal completely prevented the development of fatty livers in HT animals so fed. 3. The addition of 25 g of pancreas to the daily food intake also prevented the fatty livers. 4. The factors responsible for the accumulation of fat in the livers of hypophysectomized-thyroidectomized dogs are discussed.

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