marked diminution of its ability to trigger positive PCA reactions in mice and guinea pigs; 3 to 4 times more ME treated antibody was necessary to obtain a reaction comparable to that produced by native antibody. In the reverse PCA technique, ME treatment was without influence on the skin reaction. Therefore, the diminution of the direct PCA reaction is not the result of an impaired antigen antibody reaction, but rather the consequence of a diminished tissue fixation of ME treated antibody. Complement fixing capacity of the antibody was practically abolished by ME treatment. From this fact and from results of PCA reactions in decomplemented animals, it follows that PCA reactions in mice and guinea pigs require little, if any complement.

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Effect of Ethionine-Induced Pancreatic Damage on Intestinal Enzyme Activity of the Rat. (29276)

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Dl-ethionine, the ethyl analog of methionine, produces pancreatic exocrine damage when added to the diet of experimental animals. In the dog, this effect has been demonstrated histologically and by assay of pancreatic enzymes obtained by cannulation of the pancreatic duct(1-3). In the rat however, the effect of dl-ethionine has been demonstrated only histologically(4-7). The purpose of the present study was to evaluate alterations of intestinal pancreatic enzyme activity as an indicator of pancreatic exocrine damage.

Material and methods. Twelve male Wistar strain rats, weighing 200-225 g each, were separated into 2 equal groups. Control animals were fed a basic diet as described by Kinney *et al*(7). Test animals received dl-ethionine in a concentration of 0.5 g/100 g of basic diet. Diets and water were administered *ad lib* for a period of 25 days. At the end of this period and without prior fasting,

TABLE I. Comparison of Pancreatic Intestinal Enzyme Activity and pH Between Control and Test Animals.

	Rat #	pH	Units of enzyme activity* Trypsin	Chymotrypsin	Lipase
Control group—Basic diet	1	7.2	482	325	330
	2	7.3	130	220	220
	3	6.9	422	297	242
	4	7.5	606	404	273
	5	7.4	720	430	355
	6	7.2	520	370	230
	Mean	7.25	480	341	275
Test group—Ethionine diet	7	7.2	130	50	85
	8	7.0	140	52	144
	9	7.3	62	42	20
	10	7.5	94	38	33
	11	7.1	152	130	48
	12	6.7	100	90	38
	Mean	7.13	113	67	61

* Results are expressed as micromoles of substrate split per minute by total intestinal washings.

each rat was anesthetized with sodium pentobarbital, the abdomen was opened, the duodenum was transected at the pylorus, and the entire small intestine was removed by separating it from its mesenteric attachment. The ileum was transected at its junction with the cecum. The pyloric end was tied snugly over the flared end of a 5 cm length of polyethylene tubing which was connected to a glass syringe. Ten ml of cold 0.9% NaCl were flushed through the small intestine and the washings were collected in test tubes kept at 4°C and then stored at —20°C for several days until enzyme values were determined. Trypsin, chymotrypsin and lipase activities of the intestinal washings were measured according to the methods described by Pelot and Grossman(8). All enzyme determinations were measured titrimetrically at 37°C using a pH-stat (Radiometer Corp., Copenhagen, Denmark) and values were expressed as micromoles of substrate split per minute by the washings.

Results. The enzymatic activity of washings from the small intestine of rats fed a basic diet and those fed a diet containing dl-ethionine is compared in Table I. Results are expressed as total activity contained in intestinal washings of each rat. There was a highly significant reduction of trypsin, chymotrypsin and lipase activities in rats treated with dl-ethionine as compared with those of controls. There was no significant difference in pH values between the two groups.

Discussion. Methionine is essential for normal pancreatic exocrine function. Ethionine acts as a metabolic antagonist of methionine (9), therefore its addition to a diet would be expected to produce effects similar to methionine deficiency.

Histologic evidence of pancreatic damage has been demonstrated previously in rats fed dl-ethionine for a period of 25-30 days(4-7). Examination of tissues from our test animals likewise demonstrated marked acinar atrophy and fibrosis.

As a measure of pancreatic damage, enzyme studies have been conducted in dogs fed dl-ethionine and in rats on methionine-deficient diets. Decreased enzyme content in pancreatic juice was reported in dogs fed dl-ethionine in doses of 25 and 50 mg/kg daily for periods of 2-3 weeks(2,3). In rats, Véghelyi and Kemény demonstrated that feeding a methionine-deficient diet for 4 weeks resulted in almost complete disappearance of trypsin, chymotrypsin and lipase activity in pancreatic juice as determined by electrophoretic analysis(10). Their results suggest that complete elimination of dietary methionine represents a much greater insult to the pancreas than does addition of dl-ethionine to a diet containing methionine. Our experiment, therefore, appeared to have produced pancreatic damage of a lesser degree which was reflected in decreased values

for pancreatic enzyme activity. On this basis, and from our histologic evidence, it would appear that a quantitative indicator may be applied to measure pancreatic damage. The ethionine-treated rat provides a convenient laboratory model particularly when physical limitations prevent use of larger animals.

Summary. Rats fed dl-ethionine for 25 days showed a significant decrease in small intestinal trypsin, chymotrypsin and lipase activity when compared to controls. The results suggest that levels of intestinal enzyme activity may be used as a quantitative indicator of pancreatic exocrine damage.

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Effect of Anoxic-Ischemic Procedure on Experimental Epilepsy in the Rat. (29277)

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Surgical eradication of spontaneous epileptogenic foci in human brains and induced epileptogenic foci in animal brains has proved curative(1-3). The present study is an attempt to alter or destroy an epileptogenic focus in the rat brain by anoxia-ischemia and/or infarction, rather than surgical excision. The results indicate that the anoxic-ischemic procedure raises the low convulsive threshold of most epileptic rats.

Materials and methods. One hundred and twenty female Wistar rats (Hemlock Hollow Farms) with a mean initial body weight of 145 g (range 130-160 g) were divided into 4 groups and treated as indicated in Table I. On the first day of experiment the convulsive threshold of each rat of all groups was determined by the average number of intraperitoneal injections of pentamethylentetrazol (Metrazol), 15 mg/kg at 15 minute intervals, required to produce generalized convulsions (4). This initial convulsive threshold was used as a base line for comparison with the convulsive thresholds obtained after subsequent experimental interventions. Rats of Group A were kept as non-epileptic controls. On the second day of experiment, Groups B, C and D were made epileptic by application of 2 mm pellets of 325 mesh cobalt powder in the right frontal cortex, with the aid of a stereotaxic apparatus(4-6). A second Metrazol test was performed on all animals on the 16th day of experiment to determine the effectiveness of cobalt-induced epilepsy. On day 20, an attempt was made to produce an infarct by the anoxic-ischemic procedure in the left cerebral hemisphere of Group C and in the right cerebral hemisphere of Group D. This was accomplished by ligation of the common carotid artery of the desired side, followed immediately by exposure of the animal to nitrous oxide(7). Only 6 animals of Group C (60%) and 31 animals of Group D (32%) survived the anoxic-ischemic procedure. The