sponses to angiotonin and histamine and variable results with barium chloride and acetylcholine. Stone(10) found that TEA potentiated the motor effect of epinephrine on the seminal vesicle of the guinea pig. Finally, suggestive evidence was presented by Stutzman *et al.*(8), who reported that epinephrine-induced ventricular tachycardia was enhanced by tetraethylammonium chloride, even in spite of effective sympathetic block, and supradiaphragmatic splanchnicectomy.

Summary. 1. The potentiation by TEA of the pressor responses to epinephrine and nor-epinephrine has been demonstrated in cats with spinal cord pithed. 2. The effect of epinephrine was enhanced to a greater extent than that of nor-epinephrine. 3. This potentiation was not due to the modification of homeostatic cardiovascular reflexes.

Received June 18, 1951. P.S.E.B.M., 1951, v77.

10. Stone, C. A., 1951, unpublished data.

Effects of a Pancreatic Preparation (Viokase) in Depancreatized Cats. (18843)

W. J. TUDDENHAM AND A. E. MILMAN.* (Introduced by F. D. W. Lukens.)

From the George S. Cox Medical Research Institute, University of Pennsylvania, Philadelphia, Pa.

Substitution therapy for patients or animals which are deficient in the external secretion of the pancreas is still unsatisfactory. The various pancreatic preparations have afforded only limited replacement. Depancreatized carnivorous animals have usually been fed raw pancreas for its digestive and lipotropic effect. Even this falls far short of the normal external secretion. Recently a desiccated, defatted pancreatic powder (Viokase)† has been tried in depancreatized cats in this laboratory. The effect of this powder on the mass and fat content of the stools has been examined. Its influence on the insulin requirement has been observed because of Machella's unpublished report that the insulin requirement of a depancreatized man was increased during its administration.

Methods. Cats were depancreatized under nembutal anesthesia and the completeness of the operation confirmed by the amount of glucose excreted during fasting on the first one or 2 post-operative days. After this, a few days on insulin and penicillin put the animals in excellent condition. They were kept in metabolism cages. The daily excretion of glucose was determined and the dose of insulin adjusted accordingly. The stools of each cat were collected daily before the cages were cleaned, and were pooled for each metabolic period; the pooled samples were then dried to constant weight in a hood and analyzed for total fat by the method of Fowweather(1) adapted for use on the dried stool. Duplicate or triplicate analyses were performed on each sample.

The diet for all animals during all periods used for fat analyses (Tables I and II) was 150 g of raw horse meat daily. The studies on insulin requirement included some animals on 150 and some on 200 g of meat. The meat was quite constant in its composition. Analyses of different lots showed that it contained 73% water; 27% solids (dry weight); 20.8 g of protein per 100 g meat based on the determination of nitrogen. This means that the 150 g diet contained 31 g of protein, and 41 g dry weight. Two fat analyses showed 0.082 and 0.093 g of fat per gram dry weight of food. Based on the average of these measurements, the daily fat intake was 3.57 g per day. During the periods on Viokase, 2 level teaspoonfuls (about 3 g) of this powdered pancreas was mixed with the meat. Because of its small

* National Institutes of Health Postdoctorate Research Fellow, 1949-50.

† Manufactured by the Viobin Corp., Monticello, Ill.

1. Fowweather, F. S., *Brit. J. Exp. Path.*, 1926, v7, 7.

TABLE I. Wt and Fat Content of Feces of Cats Under Various Conditions (Diet Constant).

Condition	Cat No.	Period, days	Fecal wt Wet, g per day	Fecal wt Dry, g per day	Fecal fat excretion Conc.,* mg/g dry wt	Fecal fat excretion Amt, g/day	Fecal fat excretion % of ingested fat
Normal	M-9	9	3.5	—	—	.17†	5
	M-11	7	2	1.03	146	.15	4
	M-15	5	3	1.16	173	.20	6
	M-16	4	2.9	2.48	164	.41	12
Depancreatized receiving Viokase	M-7	8	4.3	—	—	1.73†	48
	M-7	7	10.2	4.62	309	1.43	40
	M-1	8	13.6	8.06	478	3.87	"100"
	M-14	6	13.2	9.25	495	4.58	"100"
	M-18	4	9.4	6.33	625	3.89	"100"
Depancreatized without Viokase	M-14	4	57	24.20	323	7.83	"100"
	M-23	4	24.5	8.38	234	1.96	55
	4	4	26	11.76	235	2.75	77
	8	5	42	15.35	231	3.54	99

* Avg of duplicate determinations on pooled sample of period.
† Based on analysis of fresh stool.

TABLE II. Avg Values of Fecal Wt and Fat Excretion (Diet Constant).

Condition	Fecal wt Wet, g per day	Fecal wt Dry, g per day	Fat excreted Conc., mg/g dry wt	Fat excreted Amt, g/day
Normal	2.9	1.55	161	.22
Depancreatized; on Viokase	10.7	7.24	464	3.23
Depancreatized; without Viokase	37.4	14.92	256	4.02

amount and freedom from fat this has been disregarded in the calculation of results.

Results. Table I presents the observations with and without the addition of Viokase to the constant meat diet. In both groups of depancreatized animals a marked variation in the weight and fat content of the stools was observed. The increased total and solid weight of the stools after pancreatectomy followed the pattern described in dogs by Selle and Moody(2). The most striking effect of Viokase is the reduction in the bulk and dry weight of the stools to half that of the untreated depancreatized series of animals. Table II summarizes the averages which because of their small number and wide range do not merit statistical analysis. However, the effect of Viokase on the weight of the stool is regarded as significant.

When the data on fat excretion are examined, it is seen that the concentration of fat tended to be greater in the treated series. However, the amount of fat excreted is essentially the same for both groups of depancreatized cats. This resembles the results obtained in dogs treated with pancreatin(2). The last column of Table I, which expresses the fat excreted as per cent of the ingested fat permits comparison with the results in depancreatized dogs studied by Coffey, Mann, and Bollman(3). They found that fat excretion amounted to 54 to 76% of the dietary fat. Our cats which excreted 40 to more than 100% indicate the range and irregularity of this finding.

During the administration of Viokase, the bulk of the stools was decreased without apparent alteration in fat absorption. In Cat M-14, which was studied on both regimens (Table I), the fecal nitrogen was determined. When given Viokase, this amounted to 0.4 g of nitrogen daily. Without Viokase the fecal nitrogen was 1.9 g per day. These values represent 2.5 and 12 g of protein respectively. Others have described the impaired protein absorption after pancreatectomy and its partial prevention with pancreatin(3). The single observation on Cat M-14 is in accord with these results.

The insulin requirement. In the studies

2. Selle, W. A., and Moody, I. W., *J. Nutrition*, 1937, v13, 15.

3. Coffey, R. J., Mann, F. C., and Bollman, J. L., *Am. J. Digest. Dis.*, 1940, v7, 141, 144.

TABLE III. Insulin Requirement of Depancreatized Cats.

Group*	Dietary supplement	Avg values: Meat per day, g	Insulin/day, units	Glycosuria/day, g	Initial wt, kg
A	Raw pancreas	182	9.5	3	2.3
B	Viokase	180	15.4	8.7	2.7

* A—based on 6 metabolic periods of 3 to 5 days each in 5 cats; B—based on 7 metabolic periods in 4 cats.

cited(2,3) no mention is made of the effect of any replacement treatment on the insulin requirement of depancreatized dogs. One would expect that improved digestion might influence the need for insulin and the data in Table III suggests that this is so. In Table III, group A consists of animals prepared 10 years ago when raw pancreas (50 g daily) was part of the diet. Group B is composed of animals on Viokase, some of which were not studied for fat excretion and received diets of 200 g. The average diet and body weight for each group is similar. The cats given Viokase received almost twice the amount of insulin used in group A, but in spite of this excreted nearly 3 times as much glucose in the urine. The dose of insulin varied widely in different cats (6 to 24 units per cat in the past few years in this laboratory). For this reason one must be guarded in the interpretation of such averages. Nevertheless, the number of animals and of metabolic periods suggest that there is a true and possibly striking effect of Viokase on the insulin requirement. When one surveys the reports on impaired pancreatic digestion and the relative inadequacy of available substitutes, it is not surprising that the depancreatized animal(4) and man(5) require less insulin than their counterparts (pituitary or alloxan diabetes(6,4) and clinical diabetes) in which an essentially normal external secretion is present.

The general usefulness of Viokase in depancreatized cats may be summarized. It is more convenient, and probably cheaper, to add a stable powder to the diet than to procure fresh pancreas. The steatorrhea and loss of body weight which follow pancreatectomy are perhaps better controlled than with raw pancreas. In general, Viokase has kept depancreatized cats in satisfactory condition. The effect on insulin requirement, which may be regarded as an index of improved digestion, suggests that this pancreatic preparation deserves clinical trial, especially when faulty absorption of protein is present.

Summary. A pancreatic preparation (Viokase) has been used to substitute for the external secretion in a series of depancreatized cats. It had no effect on fat absorption but diminished the bulk of the stools, probably by improving the digestion of protein. The improved digestion was accompanied by an increased requirement for insulin.

4. Thorogood, E., and Zimmerman, B., *Endocrinology*, 1945, v37, 191.

5. Gaston, E. A., *New England J. Med.*, 1948, v238, 345.

6. Marks, H. P., and Young, F. G., *J. Endocrinology*, 1939, v1, 470.

Received June 20, 1951. P.S.E.B.M., 1951, v77.

Detoxification of Alloxan by Borate.* (18844)

DAVID SELIGSON† AND HARRIET SELIGSON. (Introduced by F. D. W. Lukens.)

From the George S. Cox Medical Research Institute, University of Pennsylvania, Philadelphia.

It has recently been reported(1) that normal subjects excrete an alloxanic acid-like compound which on hydrolysis yields oxo-

* Supported by a grant from the Division of Research Grants and Fellowships of the National Institutes of Health, United States Public Health Service.

† Present address: Army Medical Service Graduate School, Army Medical Center, Washington, D. C.

1. Seligson, D., Seligson, H., Shapiro, B., Paley, R. G., Riaboff, T. and Lukens, F. D. W., *Fed. Proc.*, 1951, v10, 124.