TABLE II. Incorporation of Glycine-2-C^{14} into Guanidinoacetate and Creatine in Beef Pancreas.

Compounds added		cpm in Guanidinoacetate × 100	cpm in Creatine × 100
(a) Glycine-2-C^{14}, 37,000 cpm	.27 μmoles	239	2
+ Arginine	.95 "		
(b) *Idem* + S-adenosylmethionine	3.3 "	86	157
(c) " + S-adenosylmethionine	3.3 "	2	5
+ Ornithine	18 "		

ments had established that ornithine does not inhibit guanidinoacetate methylferase activity, these results provide further evidence that guanidinoacetate is an intermediate in the incorporation of glycine into creatine.

Discussion. It is now apparent that mammalian pancreas contains physiologically significant concentrations of both enzymes involved in the biosynthesis of creatine from arginine, glycine, and S-adenosylmethionine. Although it would appear that biosynthesis of creatine might be more efficiently carried out *in toto* in one organ (pancreas) rather than in successive steps in different organs, further work must be done before the relative importance of the 2 pathways can be assessed.

In either event, an important physiological role for pancreas in the biosynthesis of creatine precursor, guanidinoacetate, seems assured(5). Kidney, the other organ capable of participating in guanidinoacetate synthesis, may play only a supporting role in this respect, since its arginine-glycine transamidinase concentration is lower, and its arginase activity is much higher than that of pancreas.

Summary. An enzyme preparation from mammalian pancreas catalyzes the synthesis of creatine from guanidinoacetate and S-adenosylmethionine. Inasmuch as pancreas, in contrast to liver, can also synthesize the creatine precursor, guanidinoacetate, from arginine plus glycine, it would appear that pancreas may play a unique role in biosynthesis of body creatine.

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Received June 22, 1959. P.S.E.B.M., 1959, v101.

Modification of Protein Catabolism in the Anuric Dog.* (25104)

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Numerous studies have been reported on urea accumulation and survival time in anuric animals under various conditions. There have been, in general, beneficial effects from carbohydrate feeding and harmful effects from fasting or protein feeding(1). These results are presumably due to modification of the protein catabolic rate in each case. The response to testosterone has been variable, depending on diet used and presence or absence of catabolic accelerators such as tissue necrosis or

* Work done during tenure of Nat. Heart Inst. Post-Doctoral Fellowship. Supported in part by PHS Grant.

TABLE I. Results of Treatment with Hydrocortisone and Testosterone in Anuric Dogs.

	Survival time (hr)	Blood urea N (mg/100 ml)	Creatinine (mg/100 ml)	Phosphorus (mg/100 ml)
		48 hr post-op.		
Control	96 ± 17	150 ± 18	17.2 ± 7.7	9.1 ± 2.2
Hydrocortisone	*128 ± 33	*101 ± 37	* 7.5 ± 2.0	*5.6 ± 1.0
Testosterone	103 ± 22	142 ± 26	* 5.6 ± 1.0	*6.3 ± .8

* $p < .01$

infection(1). Under certain conditions, ACTH increases rate of urea accumulation in the nephrectomized rat while cortisone does not(2). Our experiments were performed to compare effects of hydrocortisone and testosterone on survival time, urea accumulation and other parameters in the anuric dog. The confounding effects of diet and hydration were excluded by experimental design. In anuric animals, serial concentrations of blood urea nitrogen were used to estimate rate of urea accumulation, and thus, protein catabolic rate(3). This technic depends on a relatively stable volume of total body water and absence of extra-renal loss of urea during period of observation.

Materials and methods. Mongrel dogs of both sexes living under ordinary kennel conditions had measurements made of their body weight, hematocrit, plasma concentration of urea, creatinine, phosphorus, sodium, potassium and CO_2 on 2 successive days. Standard laboratory methods were employed. CO_2 was measured as the "CO_2 combining power." Following the control period each dog was subjected to bilateral ureteral ligation under sodium pentothal anesthesia and assigned to one of 3 groups as described below. All dogs in all groups had daily post-operative measurements corresponding to preoperative measurements. No dog was allowed food or water post-operatively for duration of the animal's survival. *Group A.* 17 dogs served as controls and were given no drugs following surgery. *Group B.* 7 dogs were given hydrocortisone, 100 mg intravenously immediately following surgery and daily thereafter by same route. *Group C.* 8 dogs were given testosterone propionate, 50 mg intramuscularly immediately following surgery and daily thereafter.

Results. Preoperative measurements were normal in all respects. Post-operatively, there was a highly significant prolongation of survival time and a lower rate of urea accumulation in the hydrocortisone treated group. The 48-hour post-operative blood urea nitrogen concentration was used because it includes the largest number of surviving animals. The differences, however, persist at the same level of significance at 72 and 96 hours. Both hydrocortisone and testosterone treated groups showed a significantly lower serum creatinine and phosphorus concentration at 48 hours than did the controls. Means, standard deviations, and levels of significance are presented in Table I.

There were no significant differences among the groups with respect to decrement of body weight, decrement of plasma CO_2 concentration, or increment of plasma potassium concentration. The pooled means were respectively, 0.4 kg/day, 1.9 meq/l/day and 1.3 meq/l/day.

Discussion. The similarity of weight loss in the 3 groups suggests that changes in total body water were approximately equal. This observation, as well as lack of difference in hematocrits among the 3 groups rules out any major differences in total body water and plasma water. On this basis, the lower blood urea nitrogen concentrations in the hydrocortisone treated group may be assumed to represent a lower rate of protein catabolism. The action of hydrocortisone in prolonging survival time and lowering accumulation rates of urea, creatinine, and phosphorus is, therefore, in contrast to its effects in non-uremic animals. The association of a prolonged survival time with a lowered rate of urea accumulation in the hydrocortisone treated group is in accord with the widely held view that urea concentrations serve as an index of the presence of unknown, toxic protein catabolites.

The failure of testosterone to affect significantly survival times and urea accumulation may be related to duration of survival. Where-

as blood urea nitrogen concentrations in the hydrocortisone treated group rose in a linear fashion, those in the testosterone treated group showed a marked tendency to flatten out in the last day or 2 of the animal's life.

Summary. Hydrocortisone, given to anuric dogs, prolonged survival time with lower rates of accumulation for urea, creatinine and phosphorus in the serum. Testosterone in a second group of animals failed to influence survival time or urea accumulation.

Technical assistance of Gerald F. Rosenthal is gratefully acknowledged.

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Received May 14, 1959. P.S.E.B.M., 1959, v101.

Elevation of γ-Aminobutyric Acid in Rat Brain with Hydroxylamine.* (25105)

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γ-Aminobutyric acid (γABA)† has been found in all areas of mammalian central nervous system which have been subjected to analysis. A number of hypotheses have been advanced to account for a variety of physiological effects attributed to γABA(1-11), but none has received unequivocal experimental proof. The levels of γABA in brains of adult animals are relatively constant and show little variation from one animal to another in inbred strains of mice(12). Cerebral levels of γABA have been lowered in rats and mice by administration of Vit. B_6 antimetabolites and carbonyl trapping agents(10,13-15), but a sustained elevation of γABA in brains of normal animals has not been produced. Injection of massive doses of γABA into mice, cats, and rats produced no significant changes in brain levels of γABA(12,16) or electroencephalographic recordings(4). More than ½ of any trace dose of isotopically labeled γABA injected intracerebrally into mice disappeared within 2 minutes from the brain(11) and rapid labeling of other amino acids and tricarboxylic acid cycle intermediates occurred indicating that there is a rapid rate of metabolism of exogenously supplied γABA. Selection of NH_2OH for the study reported here was based upon observations which indicated that *in vitro* NH_2OH was a more effective inhibitor of the γABA-α-ketoglutaric acid transaminase than of glutamic acid decarboxylase (17-19) and might, therefore, cause an accumulation of γABA.

Methods. All experiments were performed with male rats of either Sprague-Dawley or Wistar strain. Treated animals were injected intraperitoneally with a solution containing 50 mg/ml NH_2OH (pH 7.0). The toxic effects observed after administration of NH_2OH are believed to result from methemoglobin formation(20) and involvement of central nervous system(21). To minimize the hematological effect some rats received an intraperitoneal injection containing 10 mg of MB in 0.5 ml(22). The dye was administered 10 to 20 minutes prior to treatment with NH_2OH. Control animals received no treatment. Intraperitoneal injections of physiological saline previously had no effect on levels of γABA in the brains of rats(10). One to 1½ hours after injection of NH_2OH the rats were killed by decapitation. Brain areas were removed

* This investigation supported in part by grant from Nat. Inst. for Neurolog. Dis. and Blindness, U.S.P.H.S.

† The following abbreviations have been used: γ-aminobutyric acid - γABA, hydroxylamine - NH_2OH, methylene blue - MB, triphosphorpyridine nucleotide - TPN.