dinase suggests that this organ plays an important role in the biosynthesis of body creatine. Whether or not methylation of guanidinoacetate also occurs in pancreas remains to be determined. In any event guanidinoacetate formed in the pancreas and released into the blood stream would have but a short journey *via* the portal vein to the liver, where methylation definitely can take place(2). In contrast to pancreas, the weak transamidinase activities of thymus and testis, briefly noted elsewhere(4), may be too low to be of physiological significance. It is of interest to compare the distribution of transamidinase in the mammal with that of another enzyme involved in arginine metabolism, argininosuccinase, previously known to occur in mammals only in liver and kidney(10). Argininosuccinase has recently been found in this laboratory to occur in numerous other tissues of the body, such as brain, testis, spleen, pancreas, thymus, heart, and skeletal muscle. The significance of this distribution is not known at present.

Summary. Arginine-glycine transamidinase, one of the 2 enzymes concerned with the biosynthesis of creatine from amino acid precursors, has been found to occur in high concentration in mammalian pancreas. Homogenates of dog pancreas have approximately 5 times the transamidinase activity of kidney homogenates from the same animal, on a wet weight basis. The assay systems by which these tissues were compared included (a) canavanine-ornithine transamidination, made unidirectional by the addition of a carbonyl compound to trap canaline, and (b) arginine-hydroxylamine transamidination. It is suggested that the ability to catalyze these latter two reactions is a characteristic property of transamidinases. Chemical and enzymic syntheses of hydroxyguanidine are described.

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Effect of Cortisol on Gastric Ulcers of the Shay Rat. (23923)

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Since Shay *et al.*(1) published that gastric (rumenal) ulcers could be produced by ligating the pylorus of a fasting rat, numerous studies have appeared, using this technic, on the effect of various agents on formation of such ulcers and on the composition of the gastric juice which accumulates. It has been found that following adrenalectomy, rumenal ulcers do not develop(2,3) and acid and pepsin production by the mucosa is greatly diminished(4,5). Replacement therapy with corticoids, however, results in ulcer formation (3) coincidental with the return of normal gastric secretion(5). In the present communication, we report the influence of large doses of cortisol (COL) on gastric ulcers using the Shay rat preparation.

Materials and methods. A total of 98 female rats, of an average body weight of 160 g, of the Upjohn strain (originally from Sprague-Dawley) were divided into groups of 8-10 animals. Half of these served as controls (receiving cortisol vehicle), whereas the other half were treated with cortisol. At 9:00 a.m., 48 hours prior to operation, food was removed. Pylorus ligation was performed after this period of fasting according to Shay's procedure(1); however, in order to avoid any

TABLE I. Effect of Cortisol on Rumenal Ulcers of Animals Killed at Various Times after Pylorus Ligation.

	Sham, 10 hr	3 hr	6 hr	9 hr	10 hr	12 hr
No. of animals/group	10	8	8	8	10	8
No. ulcers*/rat						
CMC	0	0	8.9	11.7	12.9	27
COL	0	0	3.6	5.1	8.3	8.6
Perforations (%)						
CMC	0	0	0	25	20	50
COL	0	0	0	0	10	13
Vol gastric juice (ml)						
CMC		5.3	8.2	10.9	9.2	10.5
COL		4.7	8.3	9.1	9.7	9.8
Pyloric ulcers Ulcer index†						
CMC						.0
COL						6.9

* Rumenal ulcers.

† "Ulcer Index" for pylorus portion of stomach is determined by calculating the sum of: incidence in % divided by 10, severity (in pluses) and No. of ulcers/rat. A maximum "ulcer index" is around 18-20.

possible trauma to the gastric mucosa due to introduction of a gastric tube, the stomach was not washed with saline at the time of ligation. Sham operation consisted of manipulating the pylorus without ligating. Water was withheld from the time of operation until sacrifice. COL was given at a dose of 10 mg in suspension in 0.2 ml of CMC (carboxymethylcellulose, Polysorbate 80, propylparaben and water) subcutaneously, once daily, starting at beginning of fasting period (total of 3 injections). Groups of animals were killed at various times after pylorus ligation (3, 6, 9, 10 and 12 hours) (Table I). At autopsy, the stomach was removed, opened along the lesser curvature for inspection, and the volume of accumulated gastric juice was measured. The rumenal (cardiac) and pyloric portions were carefully examined under a magnifier and the number of ulcers recorded. Their severity was graded according to a scale from 0 to +++.

Results. Rumenal ulcers. There was no ulcer in the sham operated animals and in those killed 3 hours after pylorus ligation (Table I). In the ligated rats receiving CMC and killed later than 3 hours, the rumen contained more and more ulcers with the progress of time. When the animals were treated with COL, the number of ulcers per animal and their severity were markedly decreased as compared with their respective controls (Fig. 1, 2). Moreover, many untreated animals had gastric *perforations* whereas the percentage was very small in COL-treated animals.

Pyloric Ulcers. Table I also indicates that the combination of fasting plus treatment with COL promoted formation of pyloric ulcers, *i.e.*, of the corpus of the stomach, in sev-

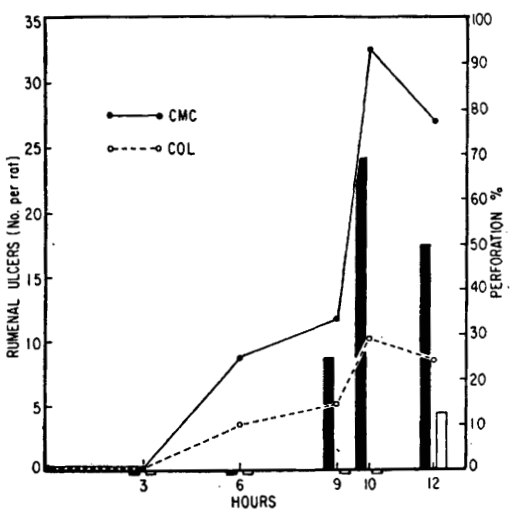

FIG. 1. No. of ulcers/animal (curves) and percentage of perforation (columns) after treatment with COL, in function of time. Black columns, controls; white columns, COL-treated animals.

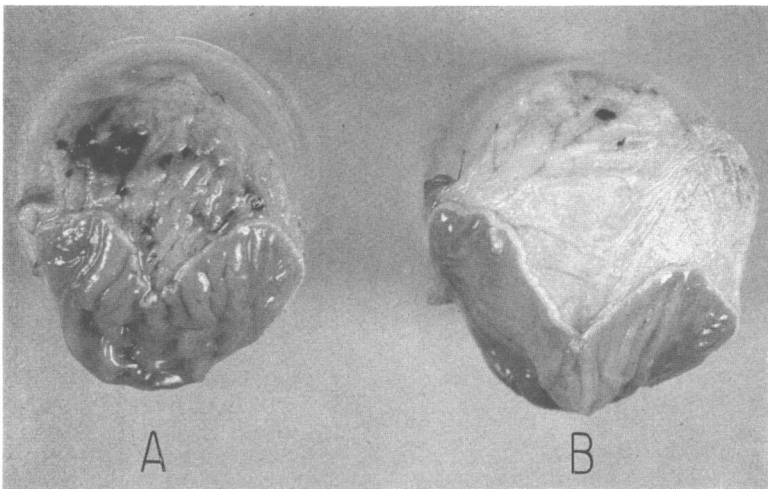

FIG. 2. Effect of COL on ulcers obtained by pylorus ligation. A. Rumenal ulcers of an untreated animal. Numerous and severe. One can see the edema of the rumen. B. Rumen of a COL-treated animal. Only a few ulcers, of moderate severity. No visible edema.

eral animals, giving, for instance, an "ulcer index" of 6.9 in the 12-hour group (see Table I for determination of "ulcer index").

Volume of gastric juice. Cortisol did not seem to influence the rate of gastric secretion following pylorus ligation.

Discussion. Cortisol markedly protected the animals against ulcerations of the rumen which are seen after pyloric ligation to the extent that perforations were rare. The mechanism of this protection is not clear, but it seems highly improbable that COL altered the composition of the gastric juice to render it less irritating to the rumenal epithelium, because of the following observations: (a) it has been shown that glucocorticoids increase peptic activity and acidity of gastric juice both in adrenalectomized rats(3,5) and in man(6); (b) urinary excretion of uropepsin in man is increased by these same hormones (6); (c) in the present experiment, the pyloric portion was ulcerated only in the groups receiving COL.

On the other hand, the protective effect of COL on the rumen might be due to its antiphlogistic property. When one examines stomachs at various times after pyloric ligation, it is striking that the first change to appear in the rumen is gross edema; histologically the edematous fluid is infiltrated with polymorphonuclears and lymphocytes, characteristic of the early stage of an inflammatory reaction. Later, necrotizing ulcers develop and the reaction becomes more severe. These morphological changes are likely to be brought about by the presence of increasing amounts of gastric juice, the latter being more irritating to the tissues than normally since there is no food to buffer its digestive activity. Therefore, it is understandable that because of its antiphlogistic property, COL blocks this inflammatory reaction (Fig. 3) and hence prevents to a large extent the formation of ulcers in the rumen. Remouchamps(7), using the Shay rat, did not observe any reduction in the number of ulcers with either ACTH or cortisone; this can be explained by the fact that he admittedly used very small doses of hormone.

The presence of pyloric ulcers following treatment with COL is reminiscent of the clinical observations that treatment with glucocorticoids is sometimes followed by gastric distress and even reactivation of ulcers. The present experiment demonstrates a paradoxical effect of COL, namely, inhibition of rumenal and development of pyloric ulcers. This strongly suggests a different mechanism for both types of ulceration. Although the Shay rat can be used with profit for the study of gastric juice under various conditions, the ulcerations obtained with this technic may not be comparable to peptic ulcers; the results of the present experiment indicate that the ru-

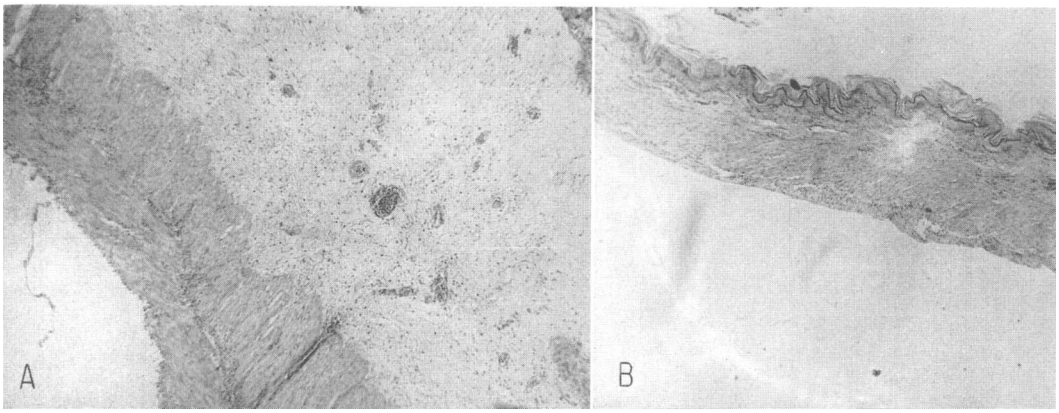

FIG. 3. Effect of COL on rumen of pylorus ligated animals. A. Rumen of untreated rat; tissues are distended by abundant edema and show marked inflammatory cell infiltration. 42 ×. B. Rumen of animal treated with COL. No edema, no inflammatory reaction. 42 ×.

men, a nonglandular structure, reacts differently than the corpus, which is the secretory portion of the stomach.

The production in the rat of ulcers in the pyloric portion following COL treatment and their expression in terms of "ulcer index" constitute the basis of an ulcer assay for steroids and will be the subject of a separate publication.

Summary. 1) Cortisol (COL) given at the daily dose of 10 mg inhibited to a large extent the development of rumenal ulcers in pylorus ligated rats. It also reduced markedly the incidence of gastric perforation. It is suggested that this protection is due to the antiphlogistic property of COL by which this hormone counteracts the initial inflammatory reaction in the rumen wall brought about normally by concentrated gastric juice. 2) At the same time, COL promoted formation of ulcers in the corpus of the stomach, whether or not the pylorus was ligated.

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Absorption of Free and Combined Fatty Acids.* (23924)

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Much evidence has accumulated to support two hypotheses that either fat must be either completely or only partially hydrolyzed to permit intestinal absorption(1). Recently, the latter of the two possibilities appears to have been more generally accepted. The reported rapid and selective absorption of labeled free fatty acids, when fed in small amounts mixed with a triglyceride(2), would make possible a transfer of mainly fatty acids across the intestinal cell wall as long as even

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