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17 Hydroxycorticosteroids in the Stomach. (27367)

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One of the main functions of the stomach is the transport of materials from the vascular side of the gastric membrane to the lumen. The primary substances moved are water and ions. The analogy between the stomach and the kidney from this aspect is obvious and suggests that the stomach may also have an excretory function.

Recently, the presence of ketosteroids in gastric juice has been demonstrated(1). The largest fraction of adrenal steroid breakdown which appears in the urine is in the form of 17 hydroxycorticosteroid substances, specifically tetrahydrocortisol and tetrahydrocortisone(2). Not all of the steroid metabolites are excreted by way of the urine(3). It is not unlikely, therefore, that the stomach could be another avenue of steroid loss.

Results from an investigation of gastric juice 17 hydroxycorticosteroid content are presented. These include the nature of the steroid and its concentration compared with blood and urine values in the same animal in control and stimulated states.

*Materials and methods.* Nine unanesthetized mongrel female dogs weighing 9.5 to 17.5 kg were studied. Three of the animals (1013, 1128, and 1223) had recovered from partial hypophysectomy (anterior lobe) performed at least one month prior to this investigation. Twenty-four hours after the last feeding, urine, blood samples, and gastric juice aspirates were obtained. Histamine\* (0.36 mg of base subcutaneously) was administered to insure an adequate stomach secretion. This constituted the control measurement for each animal. In 4 animals (1241, 1225, 1228, and 1208) after obtaining the 3 control body fluid samples, corticotropin\*\* (90 units) was infused over a 3-hour period. Gastric juice stimulated by histamine was aspirated during the last hour of corticotropin administration; urine and blood samples were obtained at the end of infusion. In the remainder of the animals a week was allowed to

\* Histamine phosphate, The Vitarine Co., Inc.

\*\*Corticotropin, Parke, Davis and Co.

## GASTRIC JUICE 17 HYDROXYCORTICOSTEROIDS

TABLE I. Gastric Juice, Blood and Urine Free 17 Hydroxycorticosteroid Concentrations in 9 Dogs under Control and Treated Conditions. Dogs 1223, 1013, and 1128 were partially hypophysectomized. Dog 1270 was treated with cortisone.

Dog No.	Free 17 hydroxycorticosteroid concentration, $\mu\text{g}/100\text{ ml}$					
	Gastric juice		Blood		Urine	
	Control	Treated	Control	Treated	Control	Treated
1241	7	11	0	15	35	50
1255	6	11	17	35	35	67
1228	4	6	19	36	36	98
1208	5*	11	27	36	28	44
1223	9	9	16	24	25	12
1013	8	14	23	30	44	34
1128	7	9	30	63	30	64
1291	8*	12	25	32	47	53
1270	8*	9	13	50	20	85
Mean	7	10	19	36	33	56
Stand. error	.5	.8	2	5	3	7

\* Samples analyzed chromatographically.

elapse between control and the period of corticotropin infusion. In one animal (1270) cortisone<sup>†</sup> (100 mg) was substituted for corticotropin.

Urine and gastric juice free 17 hydroxycorticosteroid concentrations were determined by the method of Silber and Porter(4). Blood steroid levels were measured using the method of Silber and Busch(5). In addition, the steroid content of gastric juice aspirated from 3 dogs (1208, 1291, and 1270) during the control period was analyzed chromatographically by the method of Burton *et al.* (6).

**Results.** Gastric juice contained free 17 hydroxycorticosteroid compounds in quantities which could be measured colorimetrically. The average value for the initial determinations which served as control values in 9 dogs was  $7 \pm 2^{\ddagger}$   $\mu\text{g}$  per 100 ml. Blood and urine 17 hydroxycorticosteroid levels were greater than in the gastric juice, averaging  $19 \pm 6$   $\mu\text{g}$  per 100 ml blood and  $33 \pm 9$   $\mu\text{g}$  per 100 ml urine. Administration of corticotropin induced small increases in gastric juice steroid levels in 7 of 8 dogs. Blood and urine steroid values rose considerably more under corticotropin influence. The effects of cortisone were similar to corticotropin. These results are shown in Table I.

o The 3 partially hypophysectomized dogs

<sup>†</sup> Cortisone acetate, Premo.

<sup>‡</sup> Standard deviation.

had control steroid levels similar to the intact animals in all 3 body fluid compartments. The response of the gastric juice and blood free 17 hydroxycorticosteroid concentrations to corticotropin was not different from that noted in the normal dogs. In 2 of the hypophysectomized dogs, however, urine steroid values failed to rise as a result of stimulation. This response was not seen in any normal dog.

Chromatographic analysis of 3 gastric juice aspirates revealed the presence of steroid estimated in the same concentration range as actually found colorimetrically. The mobility of the free steroid was the same as the  $R_f$  of tetrahydrocortisol. Furthermore, the steroid did not exhibit any UV absorption.

**Discussion.** These results suggest that the stomach may normally be used as an excretory route for 17 hydroxycorticosteroids. The concentration of steroid in the stomach secretions was about 20% of that found in the urine of control or corticotropin stimulated animals. Since gastric secretory volume approaches diurnal renal secretion, the amount of steroid delivered to the stomach lumen would also be about one-fifth that appearing in the urine. If the stomach steroid is allowed to pass down the gut without reabsorption, the stomach could be considered a supplemental excretory organ for steroids.

The photolorimetric determination of 17 hydroxycorticosteroids in gastric juice used

here depends on the specificity of the reaction of phenylhydrazine with the 17, 21 dihydroxy-20 keto configuration to produce compounds whose light absorption is maximal at a wave length of 410 m $\mu$ . There are other substances, such as steroids bearing the 21-hydroxy-20-keto configuration but without the 17 hydroxyl grouping which also react with phenylhydrazine. However, the absorption peaks of these substances occur at much lower wave lengths. The additional finding of a substance in gastric juice whose mobility characteristics on chromatography paralleled those of tetrahydrocortisol makes it quite likely that 17 hydroxycorticosteroids are normally present in stomach secretions.

Biliary secretion of steroid has been reported (7). Since the animals in these studies had intact stomachs and intubation was used to collect gastric juice, the possibility of bile regurgitation into the stomach must be considered. The bile has a pH nearly neutral, and its steroid levels are lower than urine concentrations. Calculation of biliary contamination sufficient to yield the 17 hydroxycorticosteroid values actually obtained in the gastric juice, assuming biliary concentrations as high as urinary levels, would result in an elevation of gastric juice pH to between 3 and 4. All gastric juice obtained in this study had a pH under 2 and gave no visual evidence of biliary contamination.

The animals with anterior lobe resections gave blood and gastric responses to corticotropin similar to the normal dogs. In 2 of these dogs urine steroids did not rise upon stimulation. At post mortem the pars anterior resections in these dogs did not include part of the stalk nor any median eminence tissue. Clinically, the effects of hypophysectomy noted in these animals were increased sensitivity to insulin, weight gain on a diet identical with their pre-operative feeding regimen and the development of a glossy coat which has been described as the result of such lesions (8). These 3 dogs were, therefore, incompletely hypophysectomized. The adrenal cortex of such animals gives a 17 hydroxycorticosteroid response to stress which ranges from nearly normal to markedly attenuated (9).

The rise in gastric juice 17 hydroxycorticosteroid levels following stimulation was small compared with urinary or blood concentration changes. Whether this indicates a rate limiting factor in gastric excretion of tetrahydrocortisol which does not exist in the kidney is not evident from these studies.

*Summary.* The free 17 hydroxycorticosteroid concentrations of gastric juice were determined in 6 normal and 3 incompletely hypophysectomized dogs and compared with urine and blood levels under control conditions and following stimulation with corticotropin or cortisone. Concentration of 17 hydroxycorticosteroid in stomach aspirates was about one-third as great as blood and one-fifth as large as urine concentrations in these animals. In 6 normal dogs steroid concentrations were considerably elevated in blood and urine and only slightly increased in gastric juice in response to corticotropin or cortisone. The urine steroid values failed to rise upon stimulation in 2 of the 3 partially hypophysectomized dogs, but the response in blood and gastric juice was comparable to the normals. The gastric juice of 3 normal dogs during the control period was analyzed chromatographically and a steroid with mobility characteristics similar to tetrahydrocortisol was found. It appears that the stomach may serve as a supplemental excretory organ for 17 hydroxycorticosteroid catabolites.

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