Effect of Catecholamines on Gastric Secretion and Blood Flow *

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THE EFFECT of epinephrine and norepinephrine on gastric secretion and ulcer provocation has remained controversial for some time. In 1908, Yukawa reported that epinephrine stimulated gastric secretion.[12] Leoper and Verpey [7] and Sirotinin confirmed his results.[10] In 1925, Ivy administered epinephrine to dogs subcutaneously and intravenously, and found both stimulation and inhibition of gastric secretion.[5] On the other hand, Rogers,[9] Hess and Grundlach,[4] Harris,[3] and others have reported that the administration of these amines inhibit gastric secretion.

Moll and Flint presented evidence that the sympathetic nervous system contains inhibitory secretory fibers to the stomach.[8] Baxter [1] found that stimulation of the sympathetics to the stomach produced a steady secretion of alkaline mucus possessing low digestive power. He also showed that the administration of epinephrine caused a 10 to 15 per cent decrease in the acidity of histamine-induced gastric secretion. In 1958, Leonsins and Waddell demonstrated in patients that the intravenous infusion of dilute norepinephrine solution decreased the volume of basal gastric secretion and secretion stimulated by peptone broth, histamine, and insulin.[6] The authors attributed this decrease in volume of secretion to vasoconstriction in the gastric mucosa.

Recently Forrest and Code reported on experiments in which they gave dogs with Heidenhain pouches sufficient histamine to induce 40–60 per cent maximal secretion.[2] Epinephrine and norepinephrine were then administered intravenously. They showed that the higher the dose of amine administered, the greater the inhibition of gastric secretion. The inhibition of gastric secretion was represented by a much greater decrease in volume than in total mEq. of acid secretion.

In the first portion of this study we investigated the effect of constant intravenous administration of epinephrine and norepinephrine amines on gastric secretion stimulated by a meat meal. In the second portion, gastric blood flow was measured during the administration of these amines.

Methods

Six adult mongrel dogs with previously constructed Heidenhain pouches were used. The standard response of the Heidenhain pouch to a cooked meat meal of 300 Gm. over a three-hour period was determined from at least 15 collections. To assess the effect of epinephrine and norepinephrine on pouch secretion, the dogs were then given a constant intravenous infusion of epinephrine and norepinephrine in the doses of 0.25, 0.5, 1.0, of 1.5 μGm./Kg./min.

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immediately after eating. The dose of amines given to each dog was alternated daily. All secretions from the Heidenhain pouches over the three hour period were measured and analyzed for pH, free acid, and pepsin. Pepsin was determined by the Anson Mirsky technic. Free acid was titrated with 0.1 N NaOH with Toepfer's re-agent as the indicator.

In dogs lightly anesthetized with sodium nembutal, gastric blood flow was measured in either the left gastric artery, or the epiploic arteries with a noncannulating gated sine wave electromagnetic flow meter (Fig. 1). Flow in the left gastric artery was measured directly while flow in the epiploic arteries was measured by placing a probe on the splenic artery after a splenectomy had been done. A control period of flow was taken for at least one hour prior to the administration of the drugs. The pulse, aortic pressure and flow response were recorded on a multi-channel recorder. The amines were infused intravenously at a rate of 0.5 or 1.0 μGm./Kg./min.

In order to visually estimate gastric mucosal blood flow, the method of Womack and Peters [11] was modified. Under light sodium nembutal anesthesia, the celiac artery and its branches were dissected. The vessels to the spleen and the hepatic artery were clamped, and 10 cc. of India ink were immediately injected into the celiac artery with just sufficient pressure to place the ink solution into the vessel lumen. The animal was sacrificed immediately with intracardiac nembutal and the stomach was removed. An average of 10 seconds elapsed between the time of ink injection and the time of gastric removal. Frozen sections (50 micron) were immediately made of the stomach and examined under the microscope. No attempt was made to quantitate the mucosal content of India ink.[10] The sections were compared to those of the control animals, and were read either as increased, or decreased. Five dogs were injected as controls. This same procedure was done during the administration of epinephrine, or norepinephrine each to five dogs at the rate of 1 μGm./Kg./min.

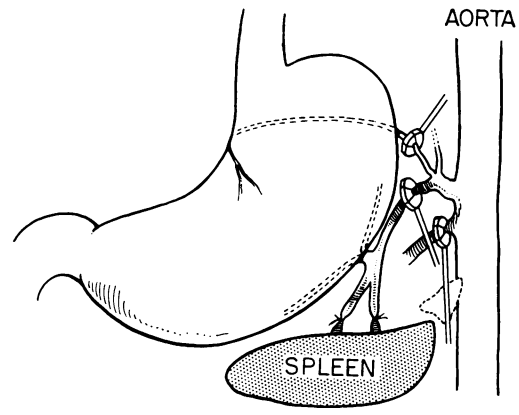

FIG. 1.

Results

In the portion of the experiment in which secretion was measured, a constant decrease in gastric secretion provoked by a meat meal was found when either epinephrine, or norepinephrine was administered (Table 1, 2). However, a consistent linear decrease in secretion with an increase in dose of amines as reported by others was not confirmed. Epinephrine or norepinephrine administered in doses greater than 0.25 μGm./Kg./min. did not

TABLE 1. *Effect of Epinephrine on Gastric Secretion*

Dog		Percentages		
		0.25μ	0.5μ	1.0μ
44	Vo.	60	54	53
	F.A.	61	67	45
4891	Vol.		58	54
	F.A.		80	60
3618	Vol.	12	34	45
	F.A.	3	43	24
3534	Vol.	50	77	66
	F.A.	84	83	93

Figures represent decrease in gastric secretion when compared to control values. Notice there is no linear correlation with dose of epinephrine administered.

TABLE 2. *Effect of Norepinephrine on Gastric Secretion*

	Control	0.5 μ/ Kg./min.	
Vol.	25.5	16	(37% ↑)
pH	1.6	2.2	
F.A.	2.65	0.73	(72% ↓)
Pepsin	0.7	0.5	

Typical response exhibited by Heidenhain pouch when norepinephrine was administered to dogs.

cause any greater inhibition than the 0.25 microgram dose. We noticed a decrease in both volume and free acid. This contrasts with previous reports that described primarily a decrease in volume with little decrease in the quantity of free acid of histamine stimulated secretion. Perhaps this disagreement can be explained by the fact that histamine is a much more potent gastric secretogogue than a meat meal.

Tables 3 and 4 show the effect of epinephrine and norepinephrine on gastric blood flow as measured in the left gastro-epiploic artery by the electro-magnetic flow meter when epinephrine or norepinephrine was given intravenously. Control blood flow in dogs under light anesthesia ranged from 2.9 to 3.7 cc./Kg. body wt./min. in the left gastric artery. It is interesting to note that the effect of epinephrine on gastric blood flow as measured by the flow meter was variable. The changes in flow are presented in these tables as per cent of the control value at the height of maximum change. Both increases and decreases in flow occur. We only attempt to explain these results by putting forth the possibility that arterio-venous shunts in the submucosal layer opened in the dogs that showed an increase in blood flow. When norepinephrine was administered, there were fairly consistent results: four of five dogs showed a decrease in left gastro-epiploic artery blood flow.

TABLE 3. *Effect of Norepinephrine on Gastric Blood Flow*

Animal	Dosage (μ/Kg./min.)	% Change	
1	0.5	36.5	↓
2	0.5	16.0	↓
3	1.0	31.0	↓
4	1.0	49.7	↓
5	2.0	23.5	↓

Effect of epinephrine on gastric blood flow was inconstant. Norepinephrine has a much more uniform effect.

The results of the India ink injections reflect the status of the mucosal capillary bed during the administration of these amines. The mucosal content of ink particles was consistently and markedly decreased in the dogs that received an intravenous infusion of epinephrine (Fig. 2). The dogs that received norepinephrine also had decreased mucosal content of ink particles (Fig. 2), which was not as marked as in the epinephrine treated dogs.

Discussion

In dogs fed a meat meal the constant infusion of epinephrine, or norepinephrine causes a decrease in gastric secretion from Heidenhain pouches. In addition, it would appear that the administration of these amines causes a decrease in gastric mucosal blood flow. It seems likely, therefore, that a factor responsible for the decrease in secretion is the decrease in blood flow to the stomach in general and to the mucosa in particular.

TABLE 4. *Effect of Epinephrine on Gastric Blood Flow*

Animal	Dosage (μ/Kg./min.)	% Change	
1	0.5	45	↑
2	0.5	30	↓
3	1.0	68.9	↑
4	1.0	75.7	↓
5	1.0	26.5	↓
6	2.0	28.1	↑
7	2.0	27.6	↑
8	2.0	5.0	↑

Effect of epinephrine on gastric blood flow was inconstant. Norepinephrine has a much more uniform effect.

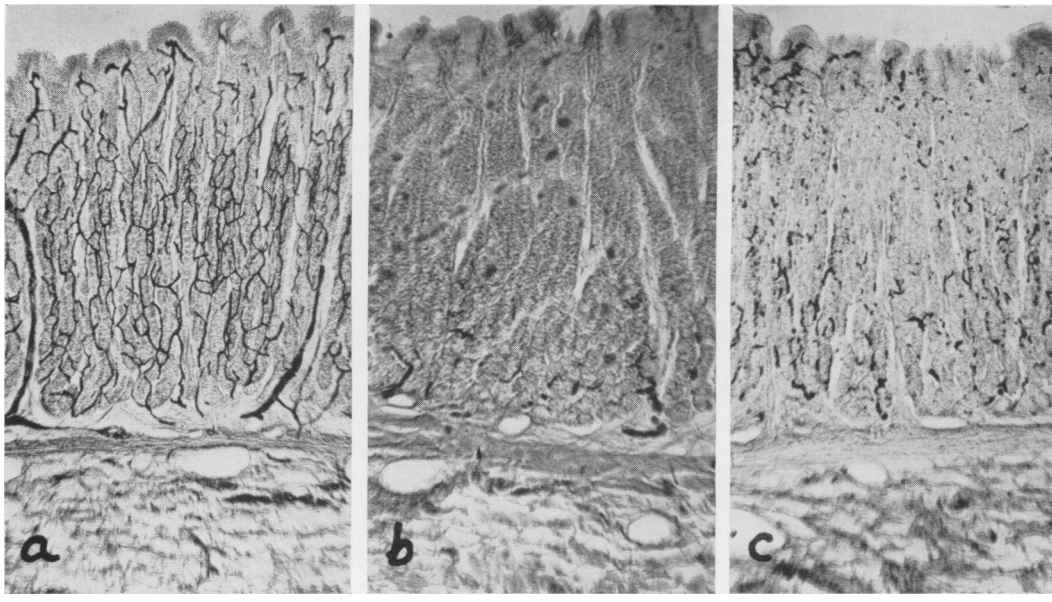

FIG. 2. a. control—the capillaries supplying the mucosa are filled with ink particles. b. During epinephrine injection nearly complete absence of filling of the capillaries in the mucosa. c. During norepinephrine injection—Considerable decrease in number of capillaries carrying blood to mucosa.

The interesting finding of a constant decrease in gastric mucosal flow with an inconsistent decrease in large vessel flow during the administration of epinephrine suggests the possibility that arterio-venous shunts open. This probably does not occur as frequently with norepinephrine since a more consistent decrease in both mucosal flow and large vessel flow was observed.

In this laboratory it has been previously observed, drugs such as histamine, reserpine, and pilocarpine which stimulate gastric secretion also increase mucosal blood flow and large vessel flow. Conversely, most agents which cause a decrease in gastric secretion are accompanied by a decrease in gastric blood flow. Although a direct effect upon the parietal cells cannot be ruled out, the data presented support the concept that epinephrine, or norepinephrine decreases gastric secretion by decreasing the amount of blood which reaches the gastric mucosa and the parietal cell.

Summary

Both epinephrine and norepinephrine inhibit gastric secretion in the dog which has been stimulated by a meat meal. Epinephrine and norepinephrine have an inconsistent effect on the total gastric blood flow. Gastric mucosal flow is decreased upon administration of intravenous epinephrine and norepinephrine inhibit gastric secretion by decreasing gastric mucosal blood flow.

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practice of surgery, medicine and the surgical specialties.

The book serves as a concise refresher course in anatomy, which should help reinforce earlier impressions and memory patterns from preclinical medical school years. A large number of easily understood illustrations amplify the text, and clarify what can be an overwhelming mass of anatomical detail in most anatomy texts.

Wherever possible, the author emphasizes anatomical landmarks which the reader can palpate on himself. In addition, practical applications of anatomical features are listed throughout the text. Almost every chapter has in an introduction, a brief review of embryologic development of the organ system being discussed. These embryologic summaries are orderly, simple and easily readable.

This book should be especially valuable for the medical student, interne, resident surgeon or practicing surgeon who needs a concise "refresher" volume to refer to for Board, licensure and other examinations.—BLAIR O. ROGERS, M.D.

ACCIDENT SURGERY, edited by H. Fred Moseley. Vol. I. Appleton-Century-Crofts, New York, 1962, $10.00.

THIS BOOK is a collection of 20 selected lectures given to the Accident Service staff of the Royal Victoria Hospital, the largest teaching hospital associated with McGill University. It is directed primarily to general surgeons, general practitioners, and other physicians who may be confronted with severely injured accident victims.

In answer to many questions which arise from the increasing number of automobile accidents, this volume is effective. One of the major aims of the editors and contributors seems to be development of pilot Accident Services in hospitals, especially smaller suburban units. Automobile accidents frequently occur in the suburbs and on country roads. Patient care on an accident service demands the greatest cooperation between general surgeon, plastic and reconstructive, orthopedic, and other specialists working together in a "team approach."

Some of the chapter headings give the reader a good indication of the scope of the volume: treatment of crushing and avulsing injuries of the hand; dashboard dislocations and acetabular fractures of the hip; extensive thermal burns; traumatic disorders of the upper extremities, arterial trauma, kidney trauma, nonpenetrating injuries of the abdomen; facial injuries in patients with multiple trauma; and head injuries in patients with multiple trauma.

There are chapters in the beginning of the volume on treatment and resuscitation of the patient at the site of the accident, transportation to the hospital, "basic" surgery of major injuries, and specific problems of anesthesia in the care of the recently injured.

This book should be especially beneficial to residents in surgery in any hospital to which automobile and other accident victims are admitted.—BLAIR O. ROGERS, M.D.

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