

undoubtedly accounts for the fact that ulcer or hematemesis have not been observed more commonly to accompany fracture of long bones in man. That fat emboli in the lung and brain are common occurrences in patients dying early after fracture of long bones is well known. In response to an inquiry addressed to 50 American orthopedic surgeons concerning the occurrence of hematemesis or ulcer after fracture, 42 replies were received. None reported observing ulcer or bleeding after fracture. However, two surgeons each reported having observed hematemesis once after the manipulation of a stiff joint under anesthesia. It has been indicated previously that the production of chronic arterial spasm also invites the occurrence of erosions and ulcer.⁸ In other words, even temporary areas of anemia in the gastric or duodenal wall

render those areas prone to injury by the gastric juice. Arterial thrombosis of gastric vessels, as well as arteriosclerosis of the terminal gastric vessels probably abet the ulcer diathesis in patients whose stomachs secrete normally. It would appear to be justifiable to suggest that bacterial emboli, lodging in the end vessels of the gastric mucosa, may also invite erosions and hematemesis

Conclusions. Fat emboli may cause gastric and/or duodenal erosions or ulcers. The presence of fat emboli after intravenous injection of fat may be demonstrated in the lung, brain, kidney and stomach. Its rate of disappearance in experimental animals is such that after 4 days it is found in sections of lung tissue in 41%, brain 11.1%, kidney 34.4% and the stomach of 3.7% of the sections examined. On the contrary, in sections of those animals sacrificed within one to four days after the intravenous injection of fat, the incidence of demonstrable fat emboli in the same tissues was: lung 91%, brain 61%, kidney 73.9% and stomach 47.8%.

⁷ Response to an inquiry addressed to 50 American orthopedic surgeons.

⁸ Baronofsky, I., and Wangenstein, O. H.. *Bull. Am. Coll. Surg.*, 1945, **30**, 59.

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Obstruction of Splenic Vein Increases Weight of Stomach and Predisposes to Erosion or Ulcer.*

IVAN BARONOFSKY AND OWEN H. WANGENSTEEN.

From the Department of Surgery, University of Minnesota Medical School, Minneapolis.

Bleeding from esophageal varices, in conditions which give rise to portal hypertension, occurs not infrequently. The usual explanation is that such bleeding has its origin in the increased hydrostatic pressure; in other words, rupture of the mucosal and submucosal veins occurs. At autopsy or operation, unusually large veins are observed commonly in the omenta of the upper end of the stomach and

about the lower end of the esophagus. Patients with obstruction of the superior vena cava, exhibiting esophageal varices, do not bleed, however. A more likely cause of bleeding, therefore, in portal hypertension would appear to be erosion by the gastric acid-peptic digestive juice. The purpose of this presentation is to test this latter thesis experimentally.

Methods. These experiments were carried out on rabbits and dogs in 3 series. In each series an obstruction to the normal venous return of part or all of the stomach to the portal system was made. In 2 of the series, the normal flow of venous blood from the left gastro-epiploic vein into the splenic was ob-

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structed by a tie placed proximal to their juncture. In the third series cellophane was placed snugly around the portal vein as it lay in the gastrohepatic omentum. Pearse¹ has shown that cellophane, when placed around the aorta, will slowly obliterate this vessel, an occurrence occasioned through the agency of a severe fibroblastic reaction within 6 weeks of the placement of the cellophane ligature. These procedures were tolerated very well by the animals, and all animals were eating and drinking normally as soon as the effects of the anesthetic wore off. After an interval of 2 days after operation in the splenic-tie series and an average of 113 days in the portal-tie series, the administration of 30 mg of the histamine-in-beeswax mixture prepared after the method of Code and Varco² was injected each evening. The dogs' feed pans were removed and no more food given until the following morning. No restriction of food intake was exercised in the instance of the rabbits. The time of sacrifice in the dogs was determined by the occurrence of spontaneous hematemesis or melena or extreme weakness. The rabbits were sacrificed at varying periods of time. In all animals the stomachs were weighed. An effort has been simultaneously made to garner control data on the weights of normal stomachs in both rabbits and dogs.

Operative Procedure. The animals were anesthetized, and under aseptic conditions a laparotomy was performed. The lesser omental bursa was entered by retracting the stomach upward and to the left; an avascular area in the omentum was opened as it came off the greater curvature of the stomach. The splenic vein was identified and dissected down to its junction with the left gastro-epiploic vein. (Fig. 1.) In the dog this is quite a constant anatomical feature. Ligatures were then placed proximal to this junction and distal to where the inferior mesenteric vein entered the splenic. The splenic vein was cut between these ligatures. The left gastro-epiploic vessels were then divided and ligated about at

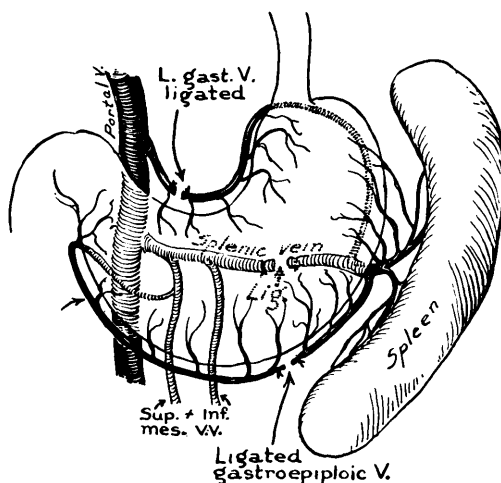


FIG. 1.

Sites of ligature of splenic, left gastro-epiploic, and left gastric vein as employed in these experiments.

the mid-point of the greater curvature. The spleen enlarged to three times normal upon ligating the splenic vein. An additional ligature and division was made of the left gastric vein on the lesser curvature before its entry into the portal vein.

In the series of experiments in which the portal vein was obstructed, the same approach was used. Upon identifying the portal vein and dissecting it for a distance of a centimeter or more, a piece of cellophane was placed snugly around it. This was knotted, care being observed that this procedure did not cause an immediate complete obstruction of the portal vein.

Experiments. Series I. Seven dogs were used in this series. The splenic vein was ligated and the histamine-in-beeswax mixture administration was begun 2 days after surgery. Two dogs in the series did not receive any histamine.

Series II. Four dogs were used in this series. The portal vein was obstructed as described above. To 2 of these 4 dogs, after a comparatively long interval (113 days), the administration of histamine-in-beeswax was commenced.

Series III. Fourteen rabbits were used. Ligature and division of the splenic vein was performed, and followed by histamine-in-beeswax administration to 9 of the 14 rabbits.

Results. The dogs with splenic-tie deteri-

¹ Pearse, H. E., *Ann. Surg.*, 1940, **112**, 923.

² Hay, L. J., Varco, R. L., Code, C. F., and Wangenstein, O. H., *Surg., Gyn. and Obst.*, 1942, **75**, 170.

TABLE I.
Production of Ulcer in Dog with Splenic-tie Followed by Administration of Histamine-in-Beeswax Mixture.

Dog No.	Wt in lb	Daily dose of histamine base, mg	No. of inj.	Results	Sacrificed after splenic-tie, days	Wt stomach, g
367	30	30	4	Large duodenal ulcer. Bleeding points and erosion in esophagus	6	210
368	44	30	2	2 large bleeding ulcers. Tremendous amt of blood in stomach	4	220
374	28	30	2	Large duodenal ulcer. 2 esophageal erosions	4	178
375	36	30	2	3 large duodenal ulcers. Esophageal erosions.	4	201.5
382	25	30	2	Stomach filled with fresh blood and clots. Fundus mucosa desquamated and sub-mucosal vessels bare.	4	193.2
Controls: (Splenic-tie but no histamine)						
362	28	0	0	No ulcers	Sacrificed 71 days after tie. Same	192
363	30	0	0	" "		201
Controls: (Histamine-in-beeswax without splenic-tie)						
1	26	30	2	No ulcers or erosions.	Sacrificed 2 days after injection started. Same Same	135.5
2	37	30	3	" " " "		131.3
3	26	30	4	" " " "		125

TABLE II.
Production of Ulcer in Dogs with Portal Vein Obstruction and Histamine-in-Beeswax Mixture.

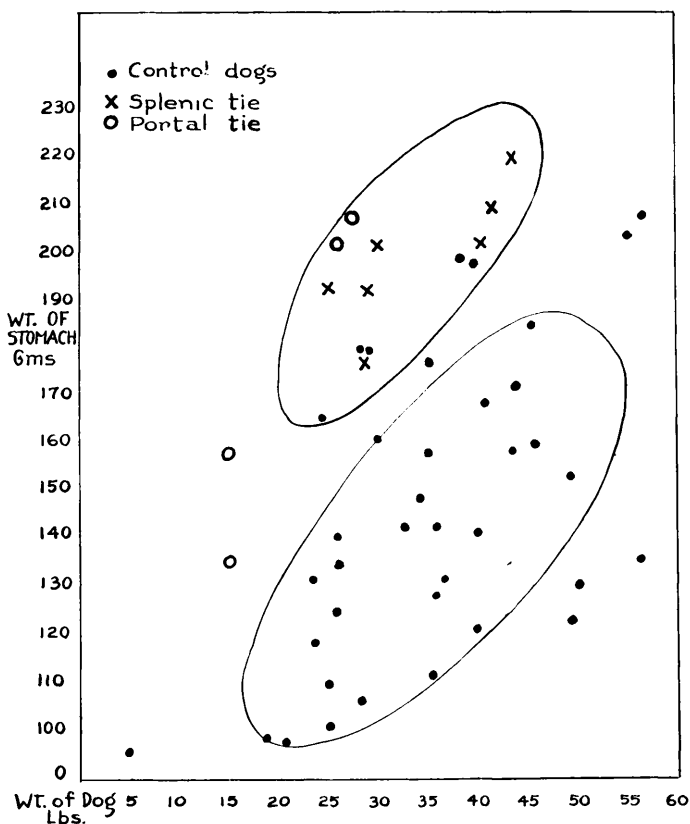
Dog No.	Wt in lb	Daily dose of histamine base, mg	No. of inj.	Results	Remarks	Wt stomach, g
317	14.5	30	2	Large duodenal ulcer. Bleeding esophageal varix.	Sacrificed 2 days after injections started.	157.5
318	15	30	3	Perforating duodenal ulcer. Multiple ulcers in stomach.	Same, 3 days after	135
Controls: (Portal vein occlusion. No histamine)						
319	26	0	0	No ulcer.	Sacrificed 101 days after operation	201.5
278	27	0	0	No ulcer. Old sub-mucosal hemorrhages in esophagus	Same, 150 days after	208

orated rapidly after the commencement of histamine administration. The average number of injections necessary to produce very large ulcers in all animals was 2.6. The results are tabulated in Table I.

The results of Series II (cellophane) are tabulated in Table II. The results parallel closely those of Series I. Examination of the scatter graph in Fig. 2 indicates definitely that the dogs with splenic or portal vein obstruction have much heavier stomachs.

There was no consistent enlargement or

fibrosis of the spleens, although in one of the control splenic-tie dogs the spleen was covered by a thick plaque of fibrous tissue, though the spleen itself was not abnormal in size. The collateral circulation in the portal obstruction series was beautifully demonstrated. The veins of Sappey, the veins of Retzius, the superior hemorrhoidal vein anastomoses, the esophageal veins, and the veins coursing through the omentum and joining the anterior abdominal wall veins were enlarged and prominent uniformly. There was minimal ascites



in one of the dogs with portal obstruction. In the 4 dogs with occlusion of the portal vein, all save one at autopsy presented complete obstruction of the vein; in that one dog, there was a small residual lumen detected only on microscopic examination.

Ulcers and/or erosions were produced in 7 out of 9 rabbits with splenic-tie followed by histamine administration. (Table III.) The stomach weights for this series averaged 32.03 g as compared with 21.4 g for the control series of normal rabbits (Table IV).

Comment. It is apparent from these experiments that obstruction of the venous drainage from the stomach abets the ulcer diathesis. That is, erosions and ulcer are far more readily provoked with histamine in the presence of portal hypertension than when there is no obstruction to venous outflow of blood from the stomach. We have been unable in the rabbit to produce ulcer with histamine alone.² However, as is indicated

herein, bleeding ulcers and erosions follow regularly when histamine administration is preceded by ligation and division of the splenic vein. Moreover, as was indicated elsewhere,³ perforated ulcers may be brought about quite regularly in the rabbit by the production of chronic arterial spasm achieved by the implantation of epinephrine in beeswax, when accompanied by the simultaneous administration of histamine.

In the dog, too, ulcer is produced regularly in a surprisingly short time when the venous drainage from the stomach is obstructed, accompanied by the administration of histamine. Esophageal varices were observed regularly in the experiments of longer duration, in which the portal vein was obstructed. Esophageal erosions were observed in several of the dogs.

³ Baronofsky, I., and Wangenstein, O. H., *Bull. Am. Coll. Surg.*, 1945, **30**, 59.

TABLE III.
Production of Ulcer in Rabbit with Splenic Vein-Tie Followed by the Administration of Histamine-in-Beeswax.

Rabbit	Size	Daily dose of histamine base, mg	No. of inj.	Results	Remarks
1	Adult	30	1	Erosions and bleeding ulcers.	Sacrificed.
2	"			Linear erosions of apices of rugæ.	Animal fasted for 2 days pre-operatively.
3	"	30	2	Erosion and bleeding ulcers.	Sacrificed.
4	"	30	1	Free blood in stomach. Enlarged varix at esophageal junction. Bleeding ulcers and erosions.	"
5	"	30	2	Bleeding ulcers and erosions.	"
6	"	30	7	Bleeding erosions at cardia.	"
7	"	30	7	No ulcers.	"
8	"	30	2	Bleeding erosions and ulcers.	"
9	"			No ulcers.	" 25 dys.
10	"	30	17	Bleeding erosions.	"
Controls: (Splenic-tie without histamine)					No histamine. Sacrificed 17 days.
11	Adult	0	0	No ulcers or erosions.	Same, 12 days.
12	"	0	0	" " " "	Same, 12 days.
13	"	0	0	" " " "	Same, 8 days.
14	"	0	0	" " " "	No splenic-tie.
Controls: (Histamine-in-beeswax without splenic-tie)					No splenic-tie, Died of histamine shock.
15	Adult	30	17	No erosions or ulcers.	No splenic-tie.
16	"	30	21	" " " "	" " "
17	"	30	21	" " " "	" " "
18	"	30	28	" " " "	" " "

TABLE IV.
Weights of Stomachs of Rabbits Subjected to Splenic Vein Ligation With or Without Histamine.

No. of rabbits	Procedure	Avg wt of rabbits, kg	Avg wt of stomachs in g
13	Splenic-tie, histamine	1.8	32.03
11	No splenic-tie, no histamine	1.8	21.4
Controls:			
4	Histamine-in-beeswax 30 mg every day for 17, 21, 21, 28 days resp. No splenic-tie.	1.8	21.3

Another striking finding was the uniform increase in weight of the stomachs of both rabbits and dogs in which obstruction to the venous outflow from the stomach had been established. Microscopically, this occurrence appears to be due to an edema of the entire gastric wall, but especially of the mucosa and submucosa. Erosion of the mucosa by acid occurs readily when the blood supply has been altered by obstructing the venous outflow. Experience with patients with occult bleeding from the alimentary tract suggests, too, that acid-peptic erosion is a frequent source of the bleeding. In this clinic we have come slowly, but definitely, to this conclusion. During the past few months one of us

(O. H. W.) has submitted two patients with portal hypertension and severe anemia from repeated hematemesis (one with, the other without cirrhosis) to extensive gastric resection (90%) with cessation of the bleeding and very gratifying results.

Conclusions. 1. Partial obstruction to the venous outflow from the stomach increases its weight in rabbits and dogs. 2. Esophageal varices can be produced by portal or splenic vein obstruction and, when histamine-in-beeswax is given to such animals, esophageal and gastric erosions and bleeding are produced. 3. Portal or splenic vein obstruction abets the ulcer diathesis.