TABLE I.
Occurrence of Stomal Ulcer Accompanying Gastric Resection of Variable Sizes (25, 50, and 75%) Carried Out on the Billroth I Plan of Operation After Administration of Histamine-in-Beeswax.

Dog No.	Wt, lb	Survival, days	Results
		Series I—25% Gastric Resection.	
356	72¼	16	4 large duodenal ulcers. One perforated.
330	45	45	Small gastric ulcer. Small duodenal erosion.
331	55	45	No ulcer.
394	30	17	2 duodenal ulcers, one perforated.
		Series II—50% Gastric Resection.	
325	45	45	Large duodenal ulcer.
333	40	45	" " "
313	34	45	" " "
262	38	45	No ulcer.
		Series III—75% Gastric Resection.	
328	33	31	No ulcer. Pregnant. Dead of uterine volvulus.
329	44	45	No ulcer
372	42	45	" "
373	55	45	" "

These experiments suggest that it is unlikely that substitution of the Billroth I for the Billroth II plan of operation, in which a short afferent duodenal loop is employed, will protect against recurrent ulcer with less sacrifice of stomach. A three-quarter resection will protect against the histamine-in-beeswax provoked ulcer, whether the operation is carried out on the Billroth I or II plan of operation.

15041

Fate of Intravenously Injected Fat: Its Role in the Production of Ulcer*

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Gastric hemorrhage as a complication of fracture has been observed in patients in this clinic.[1] In a series of 52 dogs subjected to fracture of the humerus, or to a small drill hole placed through both cortices of the humerus or curettage of the bone marrow of the shaft of the humerus after placement of the drill hole, gastroduodenal pathology (erosion and/or ulcer) was demonstrated in 21% of the dogs.[2] In dogs with gastric pouches, such procedures, as well as the intravenous injection of fat, failed to evoke evidence of stimulation of gastric secretion.[3] It was observed however that ulcer could be produced by the intravenous injection of fat, when accompanied by the administration of histamine-in-beeswax.[4] It remained to be shown, however,

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[1] Wangensteen, O. H., Merendino, K. A., and Litow, S. S., *Bull. Am. Coll. Surg.*, 1945, **30**, 58.

[2] Merendino, K. A., Litow, S. S., Armstrong, W. D., and Wangensteen, O. H., *Bull. Am. Coll. Surg.*, 1945, **30**, 58.

[3] Merendino, K. A., Litow, S. S., and Wangensteen, O. H., *Bull. Am. Coll. Surg.*, 1945, **30**, 58.

[4] Baronofsky, I., and Wangensteen, O. H., *Bull. Am. Coll. Surg.*, 1945, **30**, 59.

TABLE I.
Production of Ulcer in Rabbits with Intravenous Fat and Histamine-in-Beeswax Mixture. (30 mg of histamine-in-beeswax given intramuscularly once daily).
(Series I—Rabbits).

Rabbit No.	Size, kg	No. of injections	Amount fat I.V., cc	Results	Remarks	Path. reports B	L	K	S*
1	1.58	1	1½	Perforating ulcer greater curvature	Killed 1 day after injection.	—	+	+	+
2	1.8	2	1½	Perforating ulcer greater curvature	Killed 2 days after inj.	—	+	+	+
3	1.58	1	1½	No ulcer	Dead pulmonary embolus 1 day.	+	+	+	—
6	2.1	4	2	Entire fundus eroded away	Dead in 4 days.	—	+	+	—
7	1.8	2	1½	Duodenal ulcer	2 inj. 30 mg histamine Q.O.D. x 2. Sacrificed 4 days after last inj.	—	+	+	—
8	1.58	1	1	Perforating ulcer lesser curvature	Killed 1 day after inj.	+	+	+	—
	Controls: Intravenous fat but no histamine.								
4	1.58	0	1½	No ulcer	Sacrificed 9 days.	—	+	—	—
5	1.58	0	1½	" "	" 10 "	—	+	—	—
9	1.58	0	1½	" "	" 14 "	—	—	—	—
	Controls: Histamine but no intravenous fat.								
10	1.8	28	0	No ulcer	" 28 "	—	—	—	—
11	1.58	21	0	" "	" 21 "	—	—	—	—

* B—Brain. L—Lung. K—Kidney. S—Stomach.
— = No emboli.
+ = Fat emboli present.

whether fat can be demonstrated in the end vessels of the gastric mucosa and submucosa in animals injected with fat in which ulcer was produced by intravenous injection of fat. This study concerns itself with that item.

Method. Two series of observations were carried out on 52 animals consisting of 15 rabbits, 18 dogs, 13 cats and 6 guinea pigs. A single, intravenous injection of fat was made in all the animals. Human breast or omental fat obtained from surgical procedures and extracted with ether was used. One and one-half cc of fat per kg of body weight was injected intravenously in all animals except in the guinea pigs, in which the injection was made directly into the heart.

The observations on these 52 animals are divided into 2 series. In the first, consisting of 26 animals, the presence or absence of ulcer attending the intravenous injection of fat was noted. It should be mentioned here that only 6 rabbits among the 52 animals employed in these experiments received, in addition to the intravenous fat, a daily injection of 30 mg of histamine-in-beeswax, prepared after the method described by Code and Varco.[5]

A second series of observations was then carried out on the fate of the intravenous fat, as studied by microscopic section in the 24 of the 26 animals in Series I that received fat intravenously. Twenty-eight additional similar observations were made on 7 cats, 11 dogs, 4 guinea pigs and 6 rabbits.

Experiments: Series I. Eleven rabbits, 6 cats, 7 dogs, and 2 guinea pigs were used. Six of the rabbits received both the fat and the preparation of histamine-in-beeswax mixture. Three received fat alone and 2 received histamine alone. Of the 7 dogs, 5 received fat alone, and the remaining 2 had the left and right gastric and gastro-epiploic vessels ligated in addition to the fat injection. Both the cats and guinea pigs were submitted to intravenous fat only.

Series II. Fifteen rabbits, 18 dogs, 6 guinea pigs, and 13 cats were used. These were injected intravenously with about 1.5 cc of fat per kg of body weight and were sacrificed in

[5] Code, C. F., and Varco, R. L., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 475.

TABLE II.
Production of Ulcer in Various Animals with Intravenous Fat (No Histamine).
(Series I)

	No. of	Wt	Amt of fat	Time of sacrifice	Results	Remarks
A.	6	1 to 2 kg	1.5 to 2 cc per kg	1 to 21 days after inj. of fat	Ulcers in 2 of 6 cats. Ulcers on greater curvature of stomach of cats sacrificed 4 and 18 days after fat inj.	Both showed emboli in brain, lung, kidney. Submucosal vessels of stomach of the cat sacrificed after 18 days showed fat emboli.
B.	No. of dogs 7	8 to 10.5 kg	1.5 cc per kg	Same	One dog with bleeding duodenal ulcer 14 days after fat inj.	This ulcer occurred in one of 2 dogs that had major arteries and veins of stomach, except the short gastric branches of splenic vessels ligated.
C.	No. of guinea pigs 2	600 and 800 g	1 cc	2 and 4 days after inj. of fat	Typical gastric ulcers in the guinea pig sacrificed 2 days after fat inj.	Emboli in brain, kidney, and lung. Emboli in stomach near ulcer.

TABLE III.
Occurrence of Fat Emboli Attending the Intravenous Injection of Fat (Series I and II).

	No. of animals	Amt of fat injected cc/kg	% of tissues revealing fat emboli			
			Lung	Brain	Kidney	Stomach
		Sacrificed 1 to 4 days after fat injection.				
A.	23	1½	91	60	73.9	47.8
		Sacrificed 5 to 21 days after fat injection.				
B.	29	1½	41	11.1	34.4	3.7

periods varying from one to 21 days. Sections were taken from lung, brain, kidney and stomach and stained for fat emboli.

Results. The incidence of erosion or ulcer (gastric and/or duodenal) attending the intravenous administration of fat with or without histamine is shown in Tables I, II, and III. In Series II, in animals sacrificed within one to 4 days after the intravenous injection of fat, the occurrence of fat embolism in the various tissues was as indicated in Table III.

Discussion. These results show that fat emboli released in the blood stream may occlude the end vessels in the gastric or duodenal mucosa, causing areas of local anemia; thus these areas become susceptible to the acid-peptic digestive activity of the gastric juice. It has been shown previously in this laboratory that it is difficult, if not impossible, to produce acid peptic ulcers in the rabbit using histamine alone.[6] Yet, with a combination of histamine and fat intravenously, ulcer can be produced quite consistently. The mechanism of ulcer production undoubtedly is plugging of the end vessels to the mucosa. Even though intravenously injected fat does not stimulate nor augment gastric secretion, the resultant anemic areas in the mucosa become less resistant to injury and digestion by the acid-peptic juice than is the normal mucosa. Microscopic studies of the gastric wall of animals into which fat has been injected intravenously indicate definitely that the rate of disappearance of the fat from the mucosal and submucosal vessels is rapid. This circumstance

[6] Hay, L. J., Varco, R. L., Code, C. F., and Wangensteen, O. H., *Surg., Gyn. and Obst.*, 1942, **75**, 170.

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 Wangensteen, O. H., *Bull. Am. Coll. Surg.*, 1945, **30**, 59.

15042

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

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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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