Effect of Intragastric Temperature Changes upon Gastric Blood Flow.* (24972)

P. A. SALMON,† W. O. GRIFFEN, JR.,‡ AND O. H. WANGENSTEEN
Department of Surgery, University of Minnesota Medical School, Minneapolis

Local gastric hypothermia caused profound reduction in gastric secretion and peptic digestion(1). The results obtained in its use for management of massive gastric hemorrhage in duodenal ulcer have been reassuring (2). However, the rapid cessation of bleeding observed in these patients suggested that limitation of blood flow, as well as suppression of acid-peptic activity, was a likely participating factor in the results observed. These observations indicated the need for determining the influence of local gastric hypothermia upon blood flow in the gastric wall. No information on this subject has come to our notice. Blood flow studies by dye and radioactive tracer technics were difficult of interpretation in assessing the influence of temperature upon blood flow in an organ with so complex a source of blood supply as that of the stomach. In consequence, a simple direct method similar to that used in measurement of renal and coronary sinus blood flow was employed by which it was possible to note and measure changes in gastric flow at normothermic, hypothermic and hyperthermic temperatures.

Method. Adult mongrel dogs weighing 10 to 20 kg were operated upon under intravenous nembutal anesthesia. Fig. 1 diagrammatically illustrates the manner in which gastric venous return was virtually localized to the splenic vein. Splenectomy was performed so as to maintain the integrity of the gastric venous arcades in the hilum of the spleen. The right gastroepipolic vein was ligated near the pylorus and the splenic vein tributaries, draining the pancreas, were interrupted. In this fashion gastric venous return, with the exception of a small loss to coronary and right gastric veins, flowed through the splenic vein to the portal system. In a second group of animals all gastric veins except those tributary to the splenic were ligated, thus obliging total gastric venous return to pass through the splenic vein. Venous outflow is easily determined and is interpreted as a direct reflection of arterial inflow. The splenic vein was isolated near its confluence with the portal vein; it was divided and the arms of a "Y" shaped cannula were inserted into the ends (Fig. 1). By obstructing the proximal arm of the "Y", the entire venous flow returning through splenic vein was collected. All animals were heparinized (3 mg/kg sodium heparin) just prior to insertion of the cannula. Following completion of the preparation, a thermistor in a No. 23 hypodermic needle was imbedded in the posterior wall of the gastric corpus. The animal was allowed to stabilize for 30 minutes before experiment was commenced. Blood flow was measured during 2-minute periods; first with the stomach empty, subsequently following placement and inflation of a balloon with water at 38°C., and finally during circulation of hypothermic or hyperthermic solution through the balloon. Volumes of warm, cold and hot balloons were the same. The

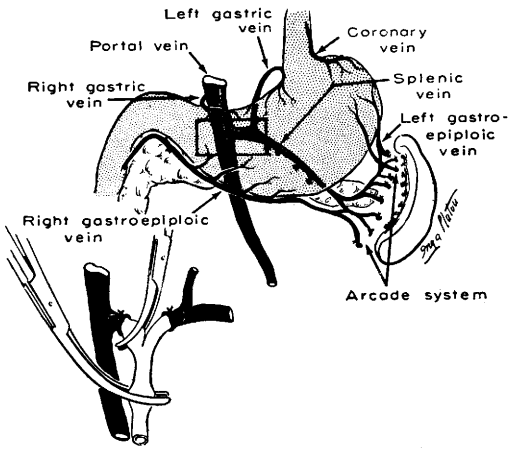

FIG. 1. Preparation for measurement of gastric venous return through the splenic vein.

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† U.S.P.H.S. Cancer Trainee.

‡ Am. Cancer Soc. Fellow.

TABLE I. Effect of Local Hypothermia on Gastric Blood Flow in 6 Dogs. (Incomplete venous isolation.) Flow—ml/min./kg of body wt.

	Stomach empty	Intragastric balloon inflated		
	S.W.* temp. 38°C	38°C	15°C	Postcooling 38°C
	2.6	2.3	.7	2.4
	2.8	2.5	.6	2.5
	2.9	2.3	1.0	2.7
	3.5	3.1	1.2	2.0
	3.2	3.0	1.1	2.9
	2.7	2.6	.7	2.4
Mean	2.9	2.6	.88	2.5
Range	2.6–3.5	2.3–3.1	.6–1.2	2.0–2.9

* S.W.—Stomach wall.

volume of collected blood was measured and blood was immediately returned to animal through a needle inserted in peripheral vein. Despite marked changes in local gastric temperature, the systemic temperature was maintained at or very near 38°C by external warming or cooling of the animals.

The *results* of experiments upon animals with incomplete gastric venous isolation are reported in Table I. Comparison of mean flows obtained under various conditions described, shows that inflation of the balloon with water at 38°C is associated with slight reduction in blood flow. When intragastric temperature was reduced to 15°C, a mean fall of 66.2% in venous outflow occurred over the 2 minute observation. Rewarming the balloon to 38°C was followed within one hour by return of flows essentially equal to precooling levels. Gradual local warming of stomach wall to 48°C resulted in increased blood flow in all but one dog (Table II). The mean increase at 48°C was 29%. Return of gastric temperature to 38°C produced a concomitant fall in blood flow.

TABLE II. Effect of Local Hyperthermia on Gastric Blood Flow in 6 Dogs. (Incomplete venous isolation.) Flow—ml/min./kg of body wt; intragastric balloon inflated.

	Temp. of stomach wall		
	38°C	43°C	48°C
	2.6	3.5	4.2
	2.6	4.4	4.4
	1.9	2.7	3.4
	3.1	3.3	3.1
	3.8	4.2	4.1
	4.4	4.5	4.8
Mean	3.1	3.7	4.0
Range	1.9–4.4	2.7–4.5	3.1–4.8

The effect of hypothermia on total gastric blood flow is shown in Table III. Mean flow, 5.9 ml/kg/minute, obtained at 38°C is about 40% higher than mean value obtained at similar temperatures in which the venous return was incompletely isolated (Tables I and II). However, depression of gastric blood flow at 15°C is essentially the same (68%) as that in Table I (66.2%). Systemic blood pressures of animals varied only slightly during experiment.

Discussion. A method has been described for estimating changes in gastric blood flow by directly measuring venous flow in the splenic vein. Although an incomplete venous return from the stomach was obtained in animals in Table I, comparison of these data with those of Table III, in which group venous outflow was complete, shows per cent reduction in flow during hypothermia to be essentially the same. The pressure within the splenic vein, taken following splenectomy, was slightly elevated, 3 to 5 cm H_2O pressure, after its cannulation. The elevated splenic vein pressure was probably related to slightly smaller lumen of the "Y" connector, as compared to the vein. Another factor helping to maintain near normal pressures within the splenic vein was the compensatory loss of splenic venous return following splenectomy. The gastric blood flow at normothermic temperatures varied somewhat from animal to animal, particularly in those in which total venous outflow was measured. The wide nor-

TABLE III. Effect of Local Hypothermia on Gastric Blood Flow. (Complete venous isolation.) Flow—ml/min./kg of body wt.

	Stomach empty	Intragastric balloon inflated	
	S.W.* Temp. 38°C	S.W. 38°C	S.W. 15°C
	5.0	5.1	1.6
	4.1	4.0	.8
	8.4	8.6	2.7
	5.2	5.0	1.6
	6.2	5.9	1.8
	7.0	6.5	2.8
Mean	5.9	5.8	1.9
Range	4.1–8.4	4.0–8.6	.8–2.8

* S.W.—Stomach wall.

mal variation in size of stomachs may account for this. Inflation of the intragastric balloon with a solution at 38°C produced only a slight decrease in blood flow. However, initiation of local gastric hypothermia with depression of temperature of stomach wall to 15°-16°C resulted in marked reduction of venous outflow. The stomach wall at these temperatures appeared blanched and slightly cyanotic. This occurrence confirms the observation that decrease in blood flow is due to cooling *per se* and not to pressure effect derived from intragastric distention.

Summary. A method has been described for estimating changes in gastric blood flow by direct measurement of gastric venous return through the splenic vein. Blood flow, attending depression of gastric wall temperature to 15-16°C was decreased by a mean value of 66.2% in those animals where some venous collateral was retained and by 68% where total venous isolation was achieved. Flows increased to 48°C. Return of gastric wall temperature to 38°C was followed by restitution of flows to approximately control levels.

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Failure of Liver to Inactivate Heparin.* (24973)

T. A. LOOMIS
Dept. of Pharmacology, School of Medicine, University of Washington, Seattle

Factors involved in terminating the action of intravenously administered heparin have not been established. The brief duration of anticoagulant action of exogenously administered heparin cannot be accounted for on the basis of excretion of the drug in urine(1). Jaques(2) described a heparin inactivating enzyme (heparinase) which he extracted from liver, but other workers(3) have presented evidence indicating that this is not a true enzyme. This report is concerned with *in vitro* and *in vivo* evidence indicating that liver is not selectively involved in terminating the action of exogenously administered heparin.

Methods. Three types of experiments were conducted using either intact mongrel dogs or dog and rabbit liver preparations. The first of these experiments was of the extirpation type in which 3 dogs were anesthetized with sodium pentobarbital (30 mg/kg), their abdomens opened, and 0.5 mg/kg of heparin injected in a saphenous vein. The anticoagulant effect was determined by Lee-White(4) 3 tube method on jugular vein blood samples. When clotting time had returned to normal, the hepatic artery, common bile duct and portal vein were ligated. The hepatic vein was clamped at its junction with the inferior vena cava and approximately 90% of liver was excised. A second dose of heparin (0.5 mg/kg) was then injected in a saphenous vein and the intensity and duration of anticoagulant action determined. The second type of experiment involved administering heparin by continuous infusion into either a branch of portal vein or a superficial saphenous vein in dogs anesthetized with sodium pentobarbital (30 mg/kg). Duration and rate of disappearance of the anticoagulant action of the drug was determined. The third type of experiment involved preparation of an aqueous extract from approximately 500 g of dog liver and from approximately 500 g of rabbit liver according to method of Cho and Jaques(5). The influence of this extract on the metachromatic action of heparin was studied *in vitro,* also according to the method of above investigators. Heparin used was from Lot. No. 4288A assaying 145.7

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