The Control of Gastrointestinal Hemorrhage by Selective Mesenteric Arterial Infusion of Vasopressin[1]

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ABSTRACT—Of 48 patients given selective mesenteric arterial infusion of vasopressin for the control of gastrointestinal hemorrhage, 28 were actively bleeding from varices secondary to portal hypertension, 14 were infused electively at the time of portosystemic shunt surgery, and 6 were infused because of hemorrhage from an arterial or capillary source demonstrated on prior selective arteriography. The indications, technique, and results of the vasopressin infusions are described.

INDEX TERMS: Gastrointestinal Tract, hemorrhage • Gastrointestinal Tract, ulcers • Hypertension, portal • Mallory-Weiss Syndrome • Portal Vein • Varices • Vasopressin

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THE INTRAVENOUS injection of vasopressin is widely used to control bleeding from esophageal varices in patients with portal hypertension. Among the disadvantages of this technique is the need for repeated doses, which may lead to tachyphylaxis and adverse cardiac reactions (1, 2).

Our previous experimental work demonstrated that vasopressin given in small amounts directly into the superior mesenteric artery decreases arterial blood flow and lowers induced portal hypertension. This decrease in portal pressure can be maintained by prolonged intra-arterial administration of vasopressin without significant cardiac or renal effects or the development of tachyphylaxis at the doses used (3).

MATERIAL, METHOD, AND RESULTS

During the past two years, we have employed selective mesenteric arterial infusion of vasopressin in 48 patients. These patients can be conveniently separated into three groups: 28 were actively bleeding from varices secondary to portal hypertension, 14 were infused electively at the time of portosystemic shunt surgery, and 6 were infused because of hemorrhage from an arterial or capillary source demonstrated on prior selective arteriography.

Group I

Vasopressin Infusion for Variceal Hemorrhage Associated With Portal Hypertension: Twenty-eight patients with massive gastrointestinal hemorrhage were studied arteriographically to locate the source of bleeding. When no source of arterial hemorrhage could be found and portal hypertension with collateral variceal channels was demonstrated, a diagnosis of bleeding from varices was made. The same catheter used for the arteriographic examination was placed in the superior mesenteric artery and continuous infusion of vasopressin was begun utilizing a Sigmomotor pump at a rate of 0.2 pressor units/ml/minute. After ten minutes of continuous infusion, a repeat superior mesenteric arteriogram was obtained using the same volume, rate of injection, and serial film programming as in the preinfusion study. After a demonstrable angiographic response was observed on the films (Figs.

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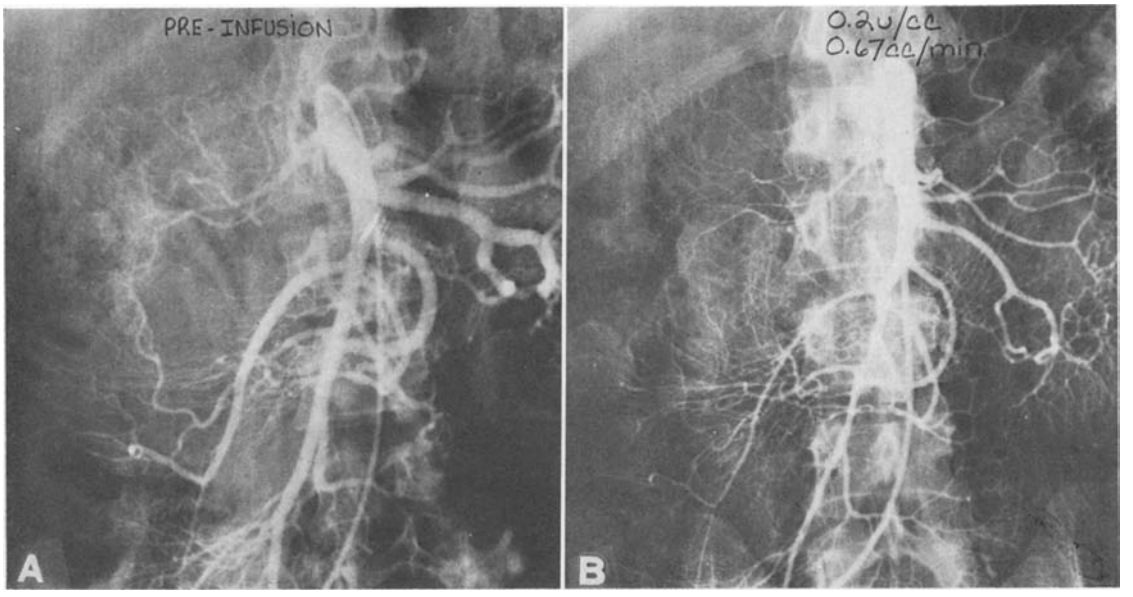

Fig. 1. A 45-year-old man with bleeding esophageal varices secondary to cavernous transformation of the portal vein. A. Preinfusion superior mesenteric arteriogram demonstrates a normal configuration of the major mesenteric arterial branches.

B. Selective superior mesenteric arteriogram during the infusion of 0.13 units/ml/minute of vasopressin into the superior mesenteric artery demonstrates moderate vasoconstriction of all major superior mesenteric artery branches. The patient stopped bleeding several minutes after the start of infusion. Infusion was continued for eight days, during which time bleeding did not recur.

1–3), the catheter was secured at the groin and the patient was transferred to his room or intensive care unit, where the infusion was maintained at the preselected rate. These 28 patients were infused for from three to fourteen days depending upon the stability of liver function and the suitability of surgical shunting.

Results: Bleeding was controlled by selective superior mesenteric arterial infusion of vasopressin in all but one of the 28 patients with active variceal hemorrhage. Of the 27 patients who were controlled, 24 underwent successful portosystemic shunting. In one patient, shunting was not possible due to previous splenectomy and cavernous transformation of the superior mesenteric and portal veins. Two patients whose bleeding was controlled by vasopressin died in hepatic coma before shunting was possible.

Group II

Vasopressin Infusion for Elective Portosystemic Shunts: Fourteen patients with portal hypertension and a history of major variceal hemorrhage underwent selective superior mesenteric arterial infusion of vasopressin, which was begun one hour prior to elective surgery and continued throughout the shunt procedure (Figs. 4 and 5). After the shunt was completed, infusions were discontinued and the catheters were removed while the patients were still in the operating room.

Results: Selective superior mesenteric arterial infusion of vasopressin during portosystemic shunt surgery resulted in a significant collapse of the collateral pathways, facilitating surgical exposure and dissection and decreasing operative time and blood loss.

Group III

Vasopressin Infusion for the Control of Arterial Bleeding: Six patients with massive gastrointestinal hemorrhage, including 2 with Mallory-Weiss tears at the cardioesophageal junction, 2 with hemorrhagic gastritis, one with a benign gastric ulcer, and one with a stress ulcer of the ascending colon, underwent selective mesenteric arteriography which successfully demonstrated the site of hemorrhage. The

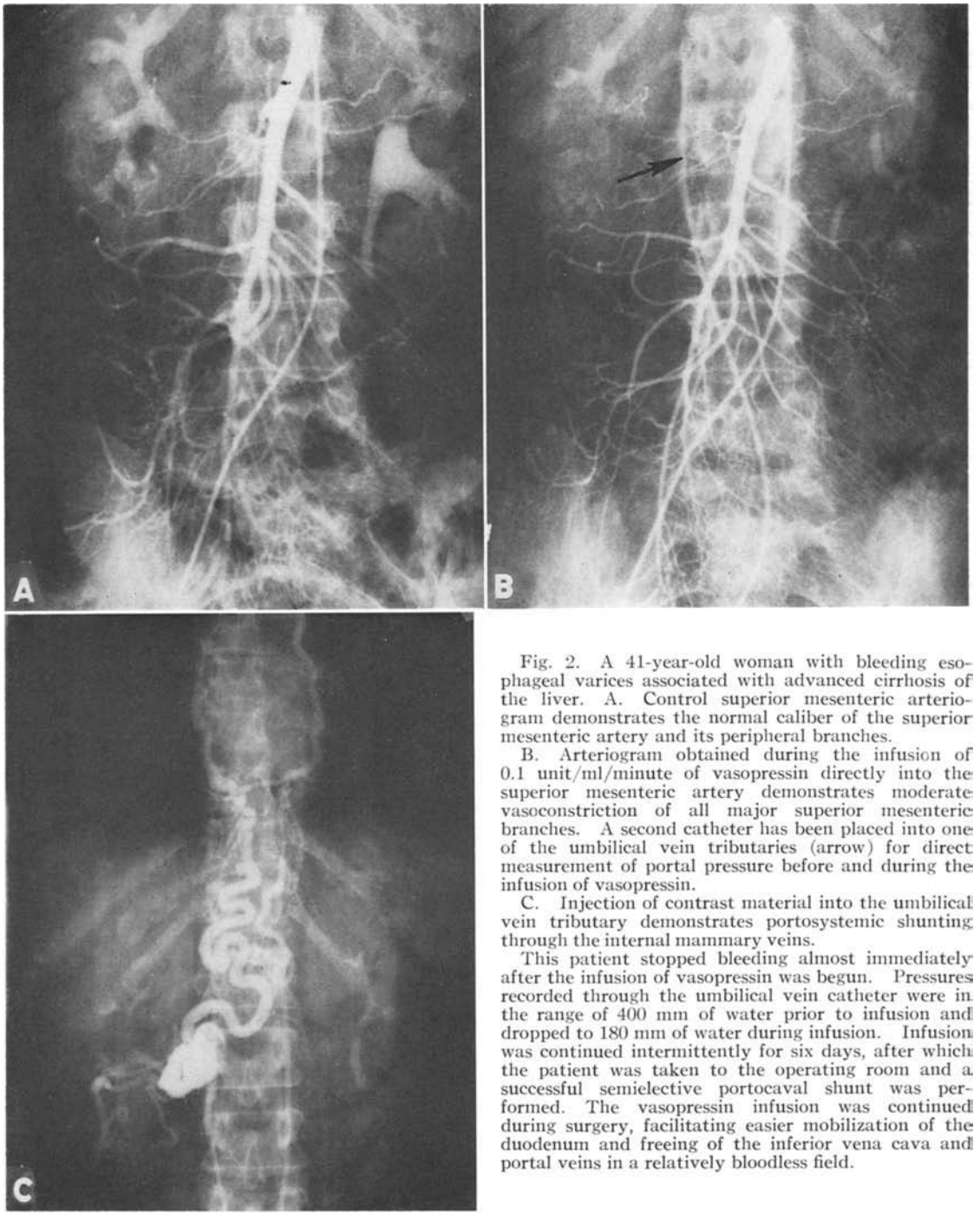

Fig. 2. A 41-year-old woman with bleeding esophageal varices associated with advanced cirrhosis of the liver. A. Control superior mesenteric arteriogram demonstrates the normal caliber of the superior mesenteric artery and its peripheral branches.

B. Arteriogram obtained during the infusion of 0.1 unit/ml/minute of vasopressin directly into the superior mesenteric artery demonstrates moderate vasoconstriction of all major superior mesenteric branches. A second catheter has been placed into one of the umbilical vein tributaries (arrow) for direct measurement of portal pressure before and during the infusion of vasopressin.

C. Injection of contrast material into the umbilical vein tributary demonstrates portosystemic shunting through the internal mammary veins.

This patient stopped bleeding almost immediately after the infusion of vasopressin was begun. Pressures recorded through the umbilical vein catheter were in the range of 400 mm of water prior to infusion and dropped to 180 mm of water during infusion. Infusion was continued intermittently for six days, after which the patient was taken to the operating room and a successful semielective portocaval shunt was performed. The vasopressin infusion was continued during surgery, facilitating easier mobilization of the duodenum and freeing of the inferior vena cava and portal veins in a relatively bloodless field.

catheter was selectively placed in the vessels supplying the area of hemorrhage and vasopressin was infused at a dose of 0.2 pressor units/ml/minute in an attempt to stop the bleeding (Figs. 6 and 7). The infusion was continued for ten minutes and the effects were observed by subsequent serial arteriography. Upward adjustment of the dose to 0.3 units/ml/minute was found to be necessary in 2 patients. The infusion was continued for two to five days, until cessation of infusion did not result in recurrent hemorrhage.

Results: Arterial bleeding was promptly

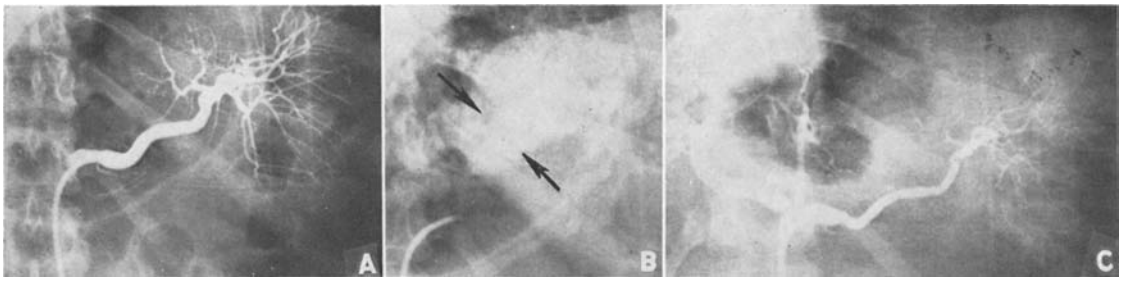

Fig. 3. A 28-year-old woman with splenic vein obstruction secondary to previous pancreatitis. The patient was studied angiographically because of massive upper gastrointestinal hemorrhage. A. Selective splenic arteriogram demonstrates a medially located spleen; no other abnormality was noted during the arterial phase of the examination.

B. The venous phase of the selective splenic arteriogram demonstrates the extravasation of contrast materia into the stomach from dilated gastric varices (arrows), confirming the clinical impression that the patient was bleeding from a gastric varix that had developed secondary to the splenic vein obstruction.

C. Because this patient was markedly obese and a very poor operative risk, "chemical splenectomy" was attempted in order to lessen the flow to the spleen and thus decrease the amount of blood coming back *via* the gastric varices. This was accomplished by infusing 0.2 unit/ml/minute of vasopressin into the splenic artery *via* the arteriographic catheter. A splenic arteriogram obtained during the infusion demonstrates marked vasoconstriction of the peripheral and main branches of the splenic artery. Because of increased peripheral resistance within the splenic artery, there was reflux into the celiac axis during arteriography, with filling of the left gastric and hepatic arteries.

The patient stopped bleeding minutes after the vasopressin infusion was begun. Bleeding did not recur, and infusion was decreased slowly over a period of four days.

controlled in all 6 patients. The 5 patients with gastric pathology required selective infusion of the left gastric artery for control of bleeding. In the sixth patient, who had a bleeding stress ulcer of the ascending colon, bleeding was controlled by infusion of vasopressin directly into the superior mesenteric artery.

DISCUSSION

During the past seven years, the authors have had substantial experience in diagnosing gastrointestinal hemorrhage by selective mesenteric catheterization (4–7). As an outgrowth of this interest, we developed techniques for the acute control of portal hypertension in patients with bleeding varices and in the control of a variety of bleeding arterial lesions by the selective arterial infusion of vasopressin at the time of the diagnostic study (8, 9).

Previous experimental studies in dogs have demonstrated the efficacy of decreasing portal pressure by infusing very small doses of vasopressin under conditions of experimental portal hypertension (3). These studies demonstrated a concomitant fall in superior mesenteric arterial flow as measured by electromagnetic flow meters at doses in the range of 0.1 pressor units/ml/minute. Cardiac output was measured using dye dilution techniques. No significant change could be measured at the dosages used. After infusions lasting up to twelve hours, histological study of the small bowel failed to demonstrate any morphological changes. Cessation of infusion resulted in the return of portal pressure and superior mesenteric arterial flow to preinfusion levels within five to ten minutes. Repeated infusions of similar doses of vasopressin failed to demonstrate any evidence of tachyphylaxis.

Using a similar series of animals, we attempted to control experimental portal hypertension by infusion of epinephrine, norepinephrine, and angiotensin. The infusions failed to produce a sustained decrease in portal pressure and superior mesenteric flow, thus supporting the work of other authors who have demonstrated an autoregulatory escape mechanism of the splanchnic circulation when vasoconstriction is mediated through the autonomic nervous system (10). The vasoconstricting effect of vasopressin infusion is independent of autonomic nervous system control and is an ideal agent for sustained infusions for this reason (11).

Serious drawbacks to the clinical efficacy of intravenous vasopressin in the control of variceal hemorrhage include decreased

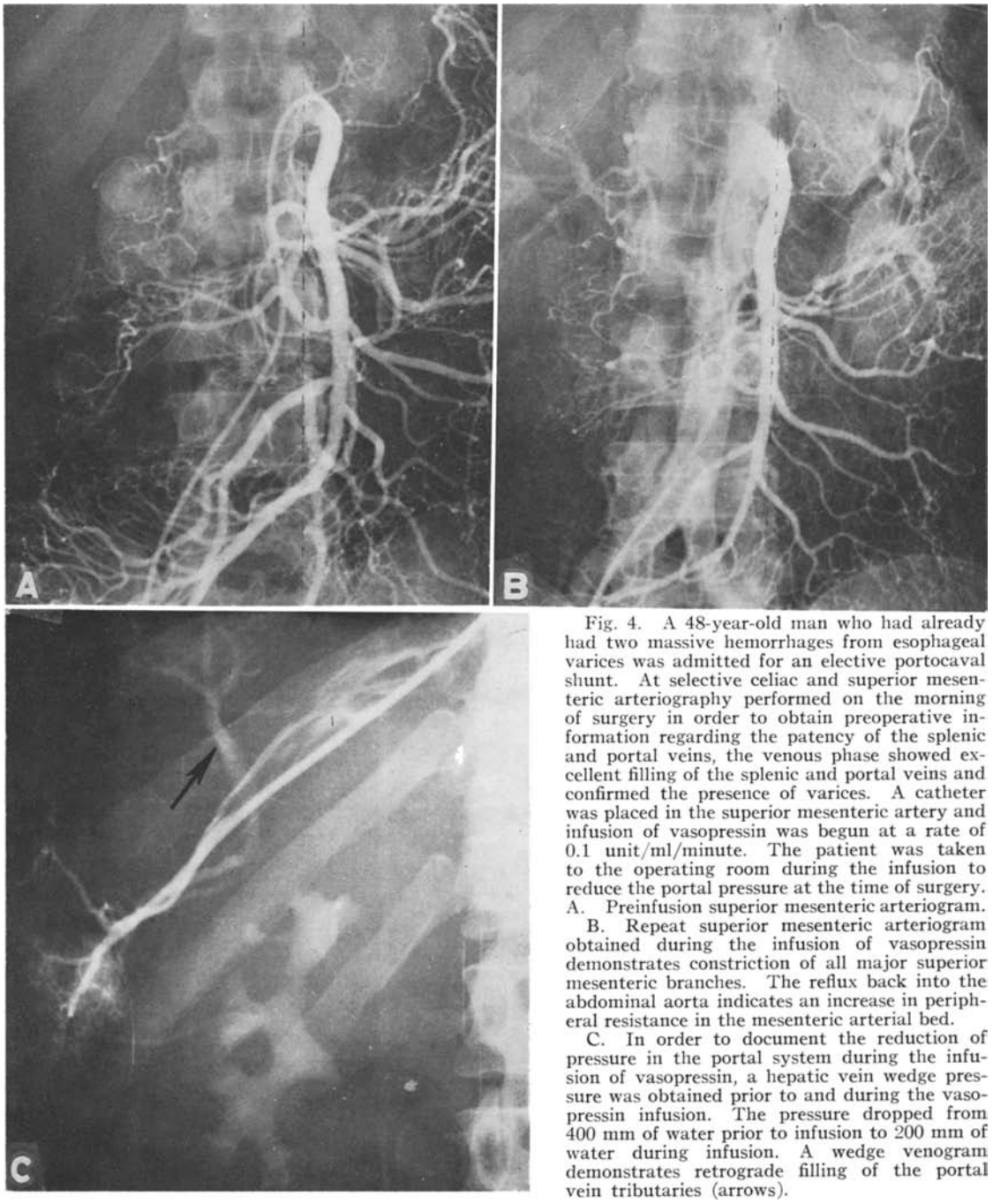

Fig. 4. A 48-year-old man who had already had two massive hemorrhages from esophageal varices was admitted for an elective portocaval shunt. At selective celiac and superior mesenteric arteriography performed on the morning of surgery in order to obtain preoperative information regarding the patency of the splenic and portal veins, the venous phase showed excellent filling of the splenic and portal veins and confirmed the presence of varices. A catheter was placed in the superior mesenteric artery and infusion of vasopressin was begun at a rate of 0.1 unit/ml/minute. The patient was taken to the operating room during the infusion to reduce the portal pressure at the time of surgery.

A. Preinfusion superior mesenteric arteriogram.

B. Repeat superior mesenteric arteriogram obtained during the infusion of vasopressin demonstrates constriction of all major superior mesenteric branches. The reflux back into the abdominal aorta indicates an increase in peripheral resistance in the mesenteric arterial bed.

C. In order to document the reduction of pressure in the portal system during the infusion of vasopressin, a hepatic vein wedge pressure was obtained prior to and during the vasopressin infusion. The pressure dropped from 400 mm of water prior to infusion to 200 mm of water during infusion. A wedge venogram demonstrates retrograde filling of the portal vein tributaries (arrows).

coronary blood flow and a subsequent fall in cardiac output as well as the rapid development of tachyphylaxis, reflecting the high doses required to achieve a pharmacological effect when an intravenous route of administration is employed. In the 48 patients arterially infused thus far, no demonstrable cardiac changes were observed. Twenty-two of these patients had prolonged infusions—some as long as ten days.

At the dosages employed, there is probably an antidiuretic effect. This was observed indirectly in one patient by prompt diuresis following cessation of infusion. As a result of this observation,

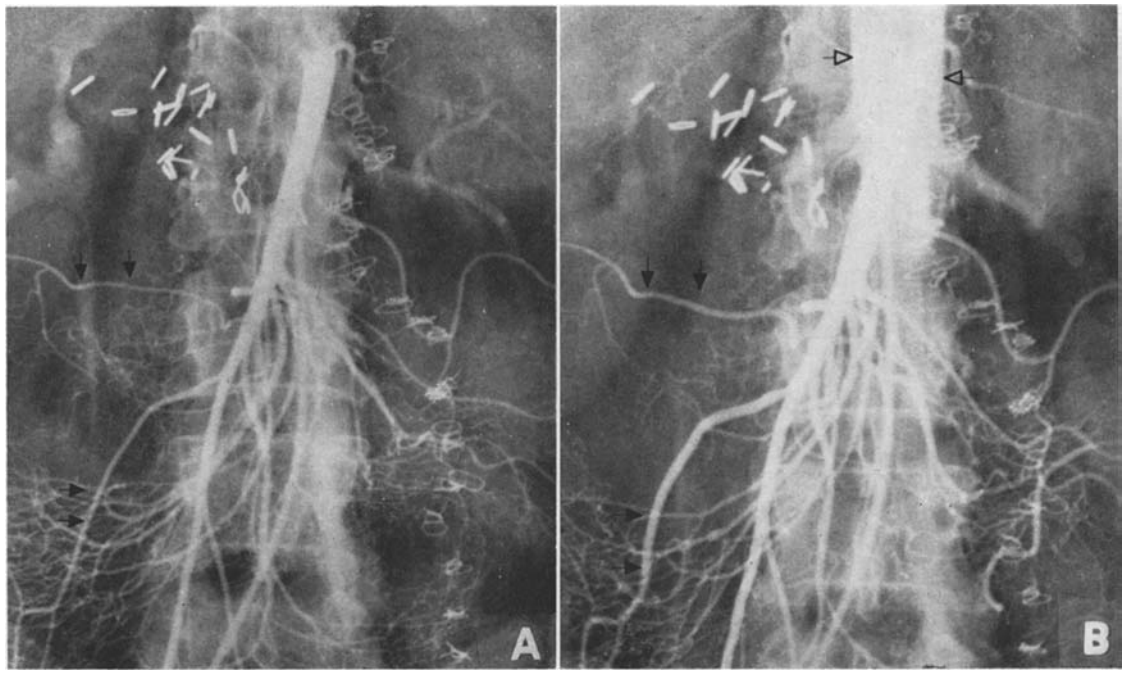

Fig. 5. Preoperative infusion of vasopressin into the superior mesenteric artery in an attempt to decrease portal pressure during portocaval shunt surgery. A. Preinfusion superior mesenteric arteriogram.
B. Superior mesenteric arteriogram obtained during the vasopressin infusion of 0.2 unit/ml/minute. Note the increase in the caliber of the proximal branches of the superior mesenteric artery (solid black arrows) as well as the reflux into the abdominal aorta (open arrows), the results of an increase in peripheral resistance. The infusion of vasopressin decreased the portal pressure by 50%.

patients with prolonged infusions are carefully observed in order to prevent fluid overload, although urinary outputs have been more than adequate during the course of the infusion. In view of our lack of knowledge of the ultimate metabolic breakdown of vasopressin, it is uncertain how much—if any—of the vasopressin administered in this fashion reaches the coronary arteries or renal tubules. Further investigation along these lines is indicated.

The final dose of vasopressin selected for continuous infusion is determined on the basis of the following arteriographic criteria:

(*a*) Vasoconstriction of the peripheral or proximal branches of the superior mesenteric artery (Figs. 1 and 2)

(*b*) The presence of increased peripheral resistance, as indicated by proximal dilatation of the superior mesenteric arterial branches associated with reflux into the abdominal aorta (Fig. 4).

Since it is important to be able to compare pre- and postinfusion arteriograms, the volume of contrast material is identical for both injections, as is the rate of injection and programming of the serial filming. To avoid obtaining a misleading postinfusion arteriogram, care is taken to empty the infusion catheter prior to the injection of contrast material to avoid injecting the vasopressin into the catheter as a bolus. This is done by using a three-way stopcock which allows for retrograde drainage of vasopressin through the catheter prior to the injection of contrast material.

Thus far, experience in experimental animals as well as patients has resulted in selection of a dose of 0.2 pressor units/ml/minute for the initial infusion. This concentration is made by mixing 100 units of vasopressin (20 units per vial)[2] and 500 ml of normal saline. This dose is infused at a rate of 1 ml/minute using a continuous-infusion Sigmomotor pump. After the infusion of 0.2 units/ml/minute for ten to fifteen minutes, an arteriogram is obtained. Depending upon the arteriographic criteria outlined above, the dose is maintained,

[2] Pituitrin, Parke-Davis, Detroit, Mich.

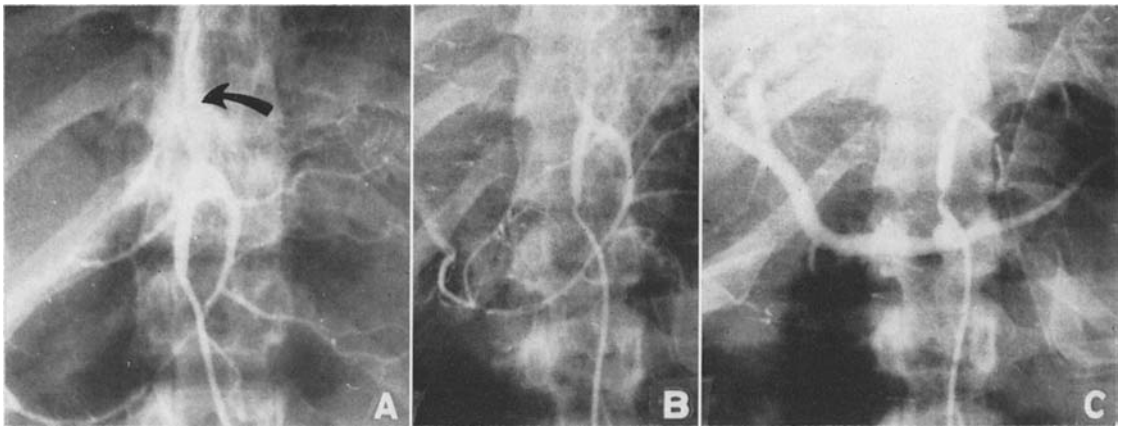

Fig. 6. Bleeding gastric ulcer controlled by the infusion of vasopressin into the left gastric artery.
A. Selective left gastric arteriogram demonstrates extravasation of contrast material on the lesser curvature of the body of the stomach (arrow); an actively bleeding ulcer was proved at surgery. Because of associated pancreatitis, extreme difficulty was encountered in mobilizing the stomach and no attempt at gastric resection, pyloroplasty, or vagotomy was made. The ulcer was sewn over and the bleeding was controlled.
B. Eight days after surgery, the patient again began to bleed massively from the upper gastrointestinal tract. Repeat left gastric arteriography was performed, and serial films again demonstrated extravasation of contrast material from a branch of the left gastric artery on the lesser curvature of the body of the stomach.
C. Repeat left gastric arteriogram obtained during the infusion of 0.2 unit/ml/minute of vasopressin into the left gastric artery demonstrates marked vasoconstriction of all branches of the left gastric artery. Note the reflux filling of the celiac axis as a result of increased peripheral resistance within the gastric artery. The bleeding stopped several minutes after infusion was begun. Infusion was continued intermittently for four days; bleeding did not recur, and the patient made an uneventful recovery.

increased, or decreased. We have not found it necessary to inject more than 0.4 units/minute to obtain vasoconstriction.

To control variceal hemorrhage secondary to portal hypertension, direct monitoring of the effectiveness of the dose in lowering portal pressure may be obtained by either umbilical vein catheterization (Fig. 2) or direct measurement of hepatic vein wedge pressure (Fig. 4). We have used both of these methods, with excellent correlation with the angiographic changes and the clinical course; and, as a result, we have frequently relied upon the angiographic changes as well as a clinical response of hemorrhage cessation without resorting to direct pressure measurements in all patients.

In a small percentage of patients, one or more branches of the hepatic artery arise from the superior mesenteric artery (12, 13). If such a variation is present, the tip of the catheter must be advanced beyond the origin of the hepatic artery in order to prevent a decrease in arterial blood flow to the liver. If there is occlusive disease at the origin of the celiac axis, the collateral flow from the superior mesenteric artery will frequently result in retrograde filling of the hepatic artery through the inferior pancreatic duodenal vessels. Care must be taken to avoid direct or indirect infusion of the hepatic artery.

The use of superior mesenteric artery vasopressin infusions during elective portosystemic shunt surgery has proved to be more effective in decreasing surgical blood loss than hypotensive anesthesia or generalized hypothermia. Both of the latter techniques have the disadvantage of decreasing hepatic arterial blood flow during the operation. Care should be taken to discontinue the infusion of vasopressin just prior to completion of the venous anastomosis in order to allow adequate portal flow during the establishment of the shunt itself.

The extension of this technique to the control of arterial hemorrhage has proved to be a promising approach to a difficult clinical problem. With angiography being used increasingly to detect gastrointestinal hemorrhage sites, it is becoming an increasingly common practice to place the catheters in the major arterial pathways

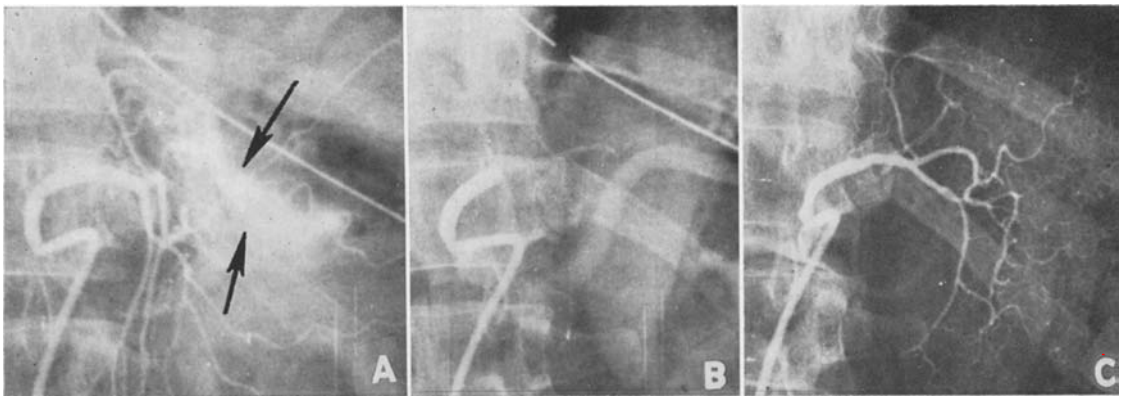

Fig. 7. Bleeding Mallory-Weiss tear at the cardioesophageal junction, controlled by the infusion of vasopressin into the left gastric artery. A. Selective left gastric arteriogram demonstrates massive extravasation of contrast material into the cardia of the stomach from a branch of the left gastric artery. Esophagoscopy confirmed the presence of an actively bleeding tear at the cardioesophageal junction.

B. Selective gastric arteriogram obtained during the vasopressin infusion of 0.6 unit/ml/minute demonstrates a complete cutoff of the midportion of the left gastric artery. This dose of vasopressin caused peripheral and proximal vasoconstriction, and the patient complained of abdominal pain at this dose level.

C. The dose of vasopressin was reduced to 0.2 unit/ml/minute. The left gastric artery now exhibits moderate vasoconstriction of the peripheral branches (as compared with Figure 7, A) without causing complete occlusion of any of the proximal branches. The bleeding was controlled at this dose, and the patient did not complain of abdominal distress. Infusion was continued for three days; the patient had no repeat episodes of bleeding and made an uneventful recovery.

from which the source of hemorrhage arises. Since the infusion of vasopressin into a major artery at the doses used clinically results in peripheral arterial vasoconstriction, we have found that superficial bleeding lesions such as a stress ulcer in the ascending colon may be effectively controlled by infusion into the superior mesenteric artery. However, if the bleeding is due to erosion into a more proximal vessel such as a branch of the hepatic or left gastric artery, infusion into the celiac or superior mesenteric artery will not be effective in controlling the bleeding. In fact, 2 patients were studied for massive hemorrhage following pancreatic and duodenal resections for carcinoma of the head of the pancreas. The site of bleeding in both was demonstrated to be the pancreatic jejunal anastomosis. Subselective infusion of vasopressin was not possible, and in both cases subsequent arteriography showed that the infusion of the celiac and superior mesenteric arteries had resulted in increased bleeding. The infusions were discontinued immediately. The control of bleeding in a proximal vessel may be accomplished if the catheter can be placed directly into the vessel leading to the bleeding artery. Direct infusion into the left gastric artery has been successful in controlling bleeding from Mallory-Weiss tears (Fig. 7), gastric ulcers (Fig. 6), and hemorrhagic gastritis. We would expect control of hemorrhage from a duodenal ulcer to require selective infusion of either the gastroduodenal or superior pancreaticoduodenal artery. There has been no evidence of mucosal damage resulting from the continuous infusion of vasopressin into the left gastric artery, even when the infusion has been maintained for six or seven days. Postinfusion arteriograms have shown that the integrity of the arterial tree is preserved.

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