Experiences with Angiography in Diagnosis and Treatment of Acute Gastrointestinal Bleeding of Various Etiologies: Preliminary Report

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VISCERAL ARTERIOGRAPHY HAS proven to be an extremely useful technic in the diagnosis of gastrointestinal bleeding. Margulis and co-workers [8] first reported in 1960 a successful operative visceral arteriography which demonstrated a bleeding cecal arteriovenous malformation. In 1963, Nusbaum, *et al.*,[11] reported the demonstration of experimentally produced bleeding points in gastrointestinal tract of dogs using the Seldinger technic of percutaneous selective visceral arteriography. In 1965, the same authors reported their experience with the successful clinical application of this method demonstrating bleeding with rates of loss as low as 0.5 ml. per minute.[12] Since that time, medical centers throughout the world have been using selective visceral angiography as an aid in the localization of gastrointestinal bleeding.

In addition to its diagnostic value the percutaneous visceral arteriography offers a new therapeutic approach to the difficult problem of massive gastrointestinal hemorrhage. Once the site of bleeding is determined, the same intra-arterial catheter can be used for selective intraluminal infusion of vasoactive drugs resulting in transient and often permanent cessation of bleeding.

The pharmacological effects of vasopressin and adrenalin on the visceral circulation were studied and described by physiologists as early as 1928 [4,9] and reviewed by Shaldon, *et al.* in 1961.[22] That knowledge prompted systemic intravenous use of vasopressin for the control of hemorrhage from esophageal varices.[6,7,20,21] In 1967, Nusbaum *et al.*, reported on selective infusion of various vasoactive substances directly into the superior mesenteric artery of dogs with experimentally produced portal hypertension.[13] These technics were then successfully utilized in treating a group of patients with massive variceal bleeding.[14] Several similar reports followed shortly confirming the efficacy of this method of treatment in other types of gastrointestinal hemorrhage.[1,2,15,16,23] Arterial gastrointestinal hemorrhage has been successfully treated also with selective intra-arterial infusion of epinephrine above or in combination with propranolol as reported by Rösch, *et al.*[17,18]

This report describes our technics and summarizes our clinical experience in selective visceral angiography used in diagnosis and treatment of acute gastrointestinal bleeding of various etiologies.

Material, Methods, and Results

During the past 2 years, 42 patients with massive, acute gastrointestinal hemorrhage were studied and treated with the use of angiography at the University of Oregon Medical School Hospitals. There were 31 males and 11 females. They ranged from 4 to 88 years of age. In all patients, the Seldinger technic of percutaneous arterial catheterization was used for both the diagnostic and therapeutic injections.

The diagnostic accuracy was excellent with only one incomplete diagnosis (Case 31). There were no deaths caused by either diagnostic or therapeutic angiography. There were three complications caused directly by the procedure. Two patients (Cases 8 & 9) had infections at the arterial catheter site associated with septicemia; both responded to removal of catheter and appropriate antimicrobial therapy. One patient (Case 27) developed a large hematoma in the groin necessitating premature removal of the catheter.

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TABLE 1. *Varices*

Case	Age Sex	Angio Diagnosis	Other Major Diagnosis	Site*	Drug*	Dose	Duration
1	56 M	Varices	ASHD—CHF Cirrhosis Alcoholism acute chronic	S.M.	P	1–28–71 0.1 μ/min 1–30–71 0.1 μ/min	18 hours 18 hours
2	62 M	Varices	Gastric ulcer Cirrhosis Jaundice Alcoholic hepatitis	S.M.	P	0.2 μ min	30 min
3	63 M	Varices	Gastric ulcer Cirrhosis	S.M.	P	0.3 μ min 0.15 μ min 0.075 μ min	1 day 3 days 1 day
4	4 M	Varices	Cavernous transformation of portal vein	S.M.	P	0.1 μ min	1 hour
5	61 M	Varices	Cirrhosis ascites P.O. Ca rectum 6–8 aspirin/day Alcoholism acute	S.M. S.M.	P P	0.15 μ min 0.3 μ min	2 hours 2 hours
6	40 F	Varices	Cirrhosis ascites Ulcerative colitis Sepsis Hypersplenism	S.M.	P	4–31–71 0.1 μ min 0.2 μ min	12 hours
7	54 F	Varices	Chronic alcoholism Cirrhosis ascites jaundice anasarca precoma	S.M.	P	0.3 μ min	1 hour
8	50 M	Varices	Alcoholism Cirrhosis ascites jaundice anasarca Carcinoma	S.M. S.M. S.M.	P P P	0.3 μ min 0.17 μ min min ?	1 hour 4 hours ?
9	59 M	Varices	Cirrhosis jaundice ascites	S.M.	P	0.3 μ min	3 hours
10	48 F	Varices	Cirrhosis jaundice ascites coma Alcoholism acute chronic	S.M.	P	0.3 μ min	2 hours
11	63 M	Varices	Cirrhosis Alcoholism Duodenal ulcer Chr. renal dis.	S.M.	P	0.2 μ min 1 hour	4 hours 0.3 μ min

Site*: S.M. = superior mesenteric
Drug*: P = pitressin

TABLE 1.—*Continued*

Follow-up		Hematologic	Surgery Time Findings Procedure	Complications	Mortality & Notes
Angio	Clinical				
No arterial bleeding	Stopped with each infusion	P & P 28%	—	1–27–71 Intractable failure 20 blood transfusions over 2 week period	Expired 2–2–71 ASHD Coronary occlusion Ventricular aneurysm Ruptured papillary muscle CHF-Pleural effusion Cirrhosis varices ascites
—	Stopped	P & P 28%	—	—	Lived 3 units transfused
—	Stopped	—	—	—	Lived 8 units transfused
—	Stopped	—	5 D elective varices Transesophageal ligation	—	Lived
—	Stopped & Rebled	P & P 67%	—	Pre coma cleared	Lived 5 units transfused
–	Stopped & Rebled Sengstaken added & stopped				
—	Slowed Stopped with Sengstaken	BSP 41% P & P 56% Fibrinogen 82.5	4–16–71 Varices Portocaval shunt (3 days after infusion)	3–31–71 Colectomy, splenectomy, iliostomy Drained ascites around iliostomy	Expired 4–26–71 Peritonitis } *Clostridium welchii* Septicemia }
—	Continued Stopped with Sengstaken	P & P 26%	—	Coma	Expired 3 days after infusion Cirrhosis coma hepatic failure
5–6–70 5–9–70 5–14–70	Stopped Stopped Stopped & Sengstaken added	P & P 60%	5–14–70 Hepatocellular Carcinoma liver on exploration	Staphylococcal septicemia & groin wound infection 5–10–70	Expired 5–20–70 Hepatocellular carcinoma liver Liver failure
10–29–70 11–8–70	Stopped Rebled 11–1–70 & Stopped with Sengstaken but rebled Stopped	P & P 74%	—	Rebled at 6 days & Sengstaken placed Ventricular tachycardia 2 hours post infusion Staphylococcic septicemia at 2 days Catheter tip positive	Expired 11–10–70 at 10 days Cirrhosis, varices, superficial ulcers stomach & duodenum Renal necrosis Hepatic failure
—	Diminished Continued Bleeding	P & P 43%	—	—	Expired 2 hours after infusion, 10 hous after admission
—	Continued bleeding even with Sengstaken placed	P & P 55%	5 hours Cirrhosis & varices Splenectomy Ligation varices	Hepatic & renal failure Sengstaken placed	Expired 3 days after surgery Cirrhosis, varices ASHD Renal nephrosclerosis

TABLE 2. *Major Ulcers*

Case No.	Age Sex	Angio Diagnosis	Other Major Diagnosis	Site*	Drug*	Dose	Duration
12	44 M	Duodenal ulcer	Alcoholism Tuberculosis Emphysema	L.G.	E	15 mcg min	20 min.
13	64 F	Duodenal ulcer	High doses aspirin ingestion	G.D.	E	—	25 min.
14	75 M	Duodenal ulcer (Fig. 3)	Bilateral pneumonia Emphysema ASHD Decubiti Cancer prostate	C	E	15 mcg min	3 hours
15	75 M	Duodenal ulcer	ASHD—CHF Alcoholism Aspirin 100/week	H	E	12 mcg min	1 hour
16	72 M	Duodenal ulcer	ASHF—A. fibrillation Rt. leg ischemia Infected leg ulcers	G.D.	E		2 hours
17	17 M	Gastric ulcer	Splenic infarct 6 mos. previously	L.G.	E	12 mcg min	30 min.
18	50 M	Gastric ulcer	270 lbs. Obese	C C C	E P E	30 mcg min 0.32 μ min 30 mcg min	1 hour 1 hour 1 hour
19	42 M	Gastric ulcer	Cirrhosis ascites jaundice Pneumonia	H	E	15 mcg min	40 min.
20	59 F	Duodenal ulcer	Plasma cell Leukemia	C S.M. H	E E E	20 mcg min 20 mcg min 20 mcg min	20 min. 20 min. 20 min.

Site*: L.G. = L. gastric; G.D. = gastroduodenal; H = hepatic; C = celiac axis; S.M. = superior mesenteric
Drug*: E = epinephrine; P = pitressin

Permanent cessation of bleeding, whether infusion was used as the only treatment or whether it was followed by elective surgery, is classified as a success. Bleeding which stopped only during the infusion, markedly diminshed bleeding, and continuous unchanged bleeding, are all considered a failure.

A constant delivery pump was used for the infusions of the vasoactive agents. The length of infusion varied from 10 minutes to 24 hours with only two patients exceeding that length (Case 3–72 hours, and Case 36–48 hours). Some patients required multiple infusions. Pitressin was used in venous variceal bleeding in doses ranging from 0.075 to 0.3 pressor units/ml./min. All patients with arterial bleeding were infused with epinephrine in doses ranging from 3–30μ/ml./min. except for one (Case 37) who was successfully infused with pitressin. Three patients were, in addition, pre-infused with propranolol, 3.0–3.5 mg. (Case 22, 23, 24). In six other patients with arterial bleeding, pitressin was added to the treatment for various reasons (Cases 18, 33, 34, 36, 39, 41).

Of the 42 patients in the study, 11 were diagnosed to be bleeding from varices. In 31, the bleeding was of arterial etiology except for two patients in the latter category (Cases 37 & 41) who bled from both sources. Patients can be conveniently separated into four groups.

Group I (Table I)

Eleven patients were bleeding from varices secondary to portal hypertension. Seven were successfully controlled with pitressin infusion and there were four failures (Cases 6, 7, 10, 11).

Group II (Table 2)

Nine patients were bleeding from a major peptic ulcer. In this group, there were six failures (Cases 12, 14, 15, 16, 18, 20).

TABLE 2.—*Continued*

Follow-up			Surgery Time Findings		
Angio	Clinical	Hematologic	Procedures	Complications	Mortality & Notes
Stopped	Stopped Rebled at 14 h.	—	14 hours Duodenal ulcer Gastritis Gastric resect.	DT's Atelectasis Liver failure	Lived 12 μ transfusion
Stopped	Stopped	—	6 days—Elect. Duodenal ulcer Gastric resect.	Abdominal wound infection	Lived
Slowed	Slowed	—	6 hours Duodenal ulcer V. & P. Tracheostomy	Extending pneumonia Stroke—Hemiplegia ASHD—Congestive failure	Died 21 days after surgery Severe bilateral pneumonia Congestive heart failure Rt. brain infarction Carcinoma prostate 6 units
Stopped	Stopped Rebled @ 2 hours	P & P 40%	2 hours Duodenal ulcer Vagotomy & Hemigastrectomy ^{B}II	Staphylococcal pneumonia CHF—Atrial pacing Pyelonephritis & Klebsiella septicemia	Lived 25 units transfused
Cont. bleeding	Cont. bleeding	P & P 40%	2 hours Duodenal ulcer Vagotomy Resection ^{B}II	Thigh amputation 3rd day Klebsiella pneumonia Klebsiella septicemia	Died 4 days after surgery Respiratory insufficiency Sepsis 8 units transfused
Stopped	Stopped	—	—	—	Lived
Cont. bleeding	Cont. bleeding	—	14 hours Gastric ulcer Gastrectomy Tracheostomy	—	Lived 6 units
Stopped (Clot put in Gastroduodenal)	Stopped	P & 31% Platelets 67,000	—	Liver & renal failure	Died 14 days after infusion Liver & renal failure antral ulcer Perforated duodenal ulcer Bilateral bronchopneumonia
Increased	Increased	Platelets 50,000 Fibrinogen 204	Minutes Duodenal ulcer Gastrectomy with ^{B}II	—	Lived 2 fresh—5 bank blood before angio at angio 6 units blood & 4 platelets Total transfusion 24 units

Group III (Table 3)

Six patients were bleeding from various major arterial sources (one marginal ulcer, one Mallory-Weiss syndrome, three colonic diverticuli and one ilial ulcer). There were no failures in this group.

Group IV (Table 4)

Sixteen patients were bleeding from stress ulcers or gastritis. There were five failures in this group.

Discussion

Systemic intravenous injection of vasopressin has been successfully used in control of variceal bleeding. It carries, however, certain risks. Large, repeated doses are often needed with frequent development of tachyphylaxis and adverse cardiovascular reactions.[20,21] The success of intra-arterial infusion of pitressin in similar situations has been at least as efficacious as intravenous infusion. With recommended clinical doses no significant tachyphylaxis, renal or cardiovascular untoward effects have been observed. Morello *et al.*,[10] has recently reported an experimental study on intra-arterial infusion of vasopressin and epinephrine. Part of the study dealt specifically with the dosage levels and side effects of these two drugs when used in dogs. Significantly, the doses of intra-arterial vasopressin or epinephrine causing side effects in dogs were determined to be 500 per cent and 600 per cent greater, respectively, than the highest doses used in this clinical study.

Rösch *et al.*, reported an experimental study comparing effects of epinephrine and pitressin on superior mesenteric arterial blood flow in dog.[17] The diminution in the rate of blood flow during the infusion was comparable with both drugs but there was a slow escape from the vasconstriction of epinephrine observed with the passage of time. (This phenomenon has been previously observed and reported by other investigators.[3,13,19]) Injec-

TABLE 3. *Mixed Arterial Bleeding*

Case No.	Age Sex	Angio Diagnosis	Other Major Diagnosis	Site*	Drug*	Dose	Duration
21	62 M	Mallory-Weiss (Fig. 2)	Alcoholism acute chronic Hiatal hernia	L.G.	E	10 mcg min	40 min
22	74 M	Diverticulosis Rt. colon (Fig. 4)	ASHD Obstructive uropathy	S.D.	Prop E	3.5 mg 15 mcg min	20 min
23	61 M	Diverticulosis Splenic flexure	Sigmoid resection 1 week previously elsewhere Transfused 30-units 18 days	I.M.	Prop E	3.0 mg 10 mcg min	10 min
24	68 M	Diverticular disease of sigmoid	Pneumonia staphylococcal pneumococcal ASHD atrial fibrillation congestive failure Gout	I.M.	Prop E	3.0 mg 10 mcg min	40 min
25	45 M	Marginal ulcer	BII—12 years P.O. ASA ingestion	C	E	30 mcg min	2 hours
26	68 M	Distal ileum	P.O. colectomy anuria sepsis	S.M.	P	0.1 μ min	15 min

Site*: L.G. = L. gastric; S.M. = superior mesenteric; I.M. = inferior mesenteric; C = celiac axis
Drug*: E = epinephrine & Prop = propranolol

tion of propranolol, a B blocker, followed by infusion of epinephrine resulted in a greater and sustained reduction in mesenteric blood flow throughout the period of the infusion. (This has been previously reported by Steckel *et al.*[24]) With epinephrine, cessation of the infusion was followed by an immediate increase in superior mesenteric flow to 110–145% of the base line level. This overshoot lasted for about 3 minutes. When pitressin infusions were stopped, the flow increased slowly reaching 80% of the base line flow in 15–40 minutes (Fig. 1). We have been using epinephrine infusion in arterial bleeding because of the rapidity and ease of controlling the rate of blood flow in the infused vessel. The slow recovery of flow following pitressin infusion and lack of knowledge as to exact fate of the drug in the body, coupled with concern over the possible harmful effects of liver infusion influenced our conservative use of pitressin.

Our current investigations in the experimental laboratory seem to indicate that following a minor transient decrease, there is actually an increase in the hepatic blood flow with direct pitressin infusion in dogs. Should this also be true in human beings, our concern about liver ischemia with pitressin infusion might be unwarranted. Nusbaum and his colleagues, in their most recent communication, reported the successful use of intra-arterial vasopressin infusion in eight patients with arterial gastrointestinal bleeding.[16] They encountered no complications. In view of the above facts and the potential cardiac and pulmonary effects of propranolol, especially in older patients, and the theoretical possibility of rebleeding during the "rebound" phase of epinephrine infusion, it may well be that intra-arterial pitressin is the drug of choice in arterial as well as venous gastrointestinal hemorrhage. Further clinical studies are presently under way at our institution.

Bleeding Esophageal Varices

There were four failures in the 11 patients bleeding from varices. One patient (Case 10), a near terminal, bleeding cirrhotic, was admitted in a coma, moribund, and probably should never have been infused. Another patient (Case 11) failed to respond to either infusion or mechanical tamponade with Linton or Sengstaken tubes. He had ligation of bleeding varices and died 3 days later in hepatorenal failure and coma. In patient 7, following 1 hour of unsuccessful infusion of pitressin, a Sengstaken tube was used which stopped the bleeding. A longer infusion might have succeeded. Similar comments can be made in Case 7. Combined use of balloon tamponade

TABLE 3.—*Continued*

Follow-up			Surgery Time Findings Procedure		
Angio	Clinical	Hematologic		Complications	Mortality & Notes
Stopped	Stopped	P & P 61%	—	—	Lived Esophagoscopy confirmed 3 units transfused
Stopped	Stopped	—	24 hrs—elective Diverticulitis Rt. hemicolectomy	—	Lived Bleeding site identified in pathologigc specimen
Stopped	Stopped	—	Hours Gastric erosion Diverticulitis V & P & ligation of bleeding point Partial colectomy	Several hours later massive upper G.I. bleeding Not studied	Lived Reanastomosis colon 3 months later
Stopped	Stopped	—	—	—	Lived Transfused 6 units
Stopped	Stopped	—	Elective 9 days No ulcers found Vagotomy	—	Lived Upper G.I. study revealed marginal ulcer Transfused 4 units
Stopped	Stopped	—	—	—	Died 32 days after infusion Acute tubular necrosis Bilateral pneumonia Hepatic failure

and pitressin infusion in Case 5, even though experimentally not pure, cannot be condemned as it resulted in the cessation of bleeding. Four patients with varices (Cases 1, 5, 8, 9) and patients 37 and 40 with stress ulcers and/or gastritis required several infusions before control of their bleeding was achieved. These infusions were relatively short—from 10 minutes to 5 hours. It seems possible that one prolonged infusion might have succeeded where several short ones failed. Our concern about the duration of the infusion and possibility of arterial thrombosis may have been overemphasized. Percutaneous intra-arterial catheters have been left in place without serious complications for as long as 2 weeks in chemotherapeutic infusions in cancer patients.[5,25] In a recent series of patients treated for arterial gastrointestinal bleeding, Nusbaum *et al.*, reported no complications as a result of leaving the infusion catheter in the left gastric artery for up to 5 days.[16] The same authors controlled 27 of 28 patients with variceal hemorrhage by infusing pitressin into superior mesenteric arteries for up to 14 days.[2] Thus, it seems that longer infusion can be more successful and yet relatively safe.

Seven of the variceal bleeders eventually died, and we feel their mortality was most probably not preventable. In this group, we may have influenced survival of two to four patients (Cases 2, 3, 4, 5) by the use of the infusional therapy.

Major Peptic Ulcer

In nine patients bleeding from a major peptic ulcer, the infusional therapy was disappointing as only three stopped with infusion. All three were relatively young; one was 17 (Case 17), one was 42 (Case 19), and one was 64 years of age (Case 13). Most of the patients who failed had marked arteriosclerosis which in combination with scarring and induration of the ulcer bed resulted in ineffective vasoconstrictive stimulus. All failures of vasoconstrictive treatment underwent prompt operation which resulted in cessation of bleeding. One of the patients who failed to stop bleeding (Case 20) had plasma cell leukemia with low platelets and decreased fibrinogen level. Another patient (Case 19) had low P & P (39%) and low platelets (67,000), and stopped bleeding only after a thrombus was infused through the catheter. Three patients in this group died (Cases 14, 16, 19). Their mortality was considered due to concomitant disease. We may have influenced the survival of one patient in this group by making his operation elective (Case 2).

All six patients in Group III, bleeding from various arterial sources, were successfully treated with the infusional therapy and all but one lived. Patient 26 died. of the primary disease. It is important to recognize the value of diagnostic localization of the source of colonic bleeding (as exemplified by our Cases 22, 23, 24). In the

TABLE 4. *Gastritis and Superficial Ulcers*

Case No.	Age Sex	Angio Diagnosis	Other Major Diagnosis	Site*	Drug*	Dose	Duration
27	66 F	Stress ulcers	Emphyema gallbladder Sigmoid volvulus Quadriplegia	L.G.	E	8 mcg min	30 min.
28	62 F	Stress ulcers	HCVD & ASHD—CHF Diabetes mellitus Chr. renal dis. CVA—1963	L.G.	E	20 mcg min	30 min.
29	67 M	Gastritis	Alcoholism acute chronic RHD Class IV	H	E	—	30 min.
30	38 M	Gastritis	Alcoholism acute chronic	C	E	18 mcg min	40 min.
31	28 F	Stress ulcers	Cirrhosis varices Alcoholism acute chronic Tuberculosis	H	E	8 mcg min	20 min.
32	63 M	Stress ulcers	P.O. aortic graft ASHD Chronic renal disease	L.G.	E	10 mcg min	30 min.
33	47 M	Stress ulcers	Alcoholism Cirrhosis jaundice ascites Chronic renal disease	L.G.	E	3 mcg min	1 hour
34	68 M	Stress ulcers	Biliary sepsis Cholangitis	C C	E P	11–18–71 20 mcg min 0.2 μ min	30 min. 22 hours
35	79 F	Multiple ulcers	Myeloproliferative disorder Prednisone 30 mg daily	H S.M.	E P	4–18–71 ?	2 hours
36	63 M	Stress ulcers Jejunal ulcer	Gastrectomy 1963 Alcoholism cirrhosis Luetic —meningovasc. —aneurysm —neurogenic bladder Tuberculosis	C	E	8–28–70	30 min
37	61 M	Gastritis	P.O. colectomy Oral squamous carcinoma ASHD with pacemaker Uremia Resp. insufficiency Sepsis	L.G.	E P	5–3–71 240 mcg 80 +	? 48 hours

TABLE 4.—*Continued*

Follow-up			Surgery Time Findings		
Angio	Clinical	Hematologic	Procedure	Complications	Mortality & Notes
Stopped	Stopped	—	—	Cholecystostomy 10–26 Monilia septicemia 11–4 Tracheostomy 11–7	Lived Angio 11–3 4 units blood
Stopped	Stopped Rebled	—	Hours? Fundic stress ulcer Vagotomy Vagotomy Gastroenterostomy	Large hematoma around catheter Pneumothorax P.O. Myocardial infarction	Lived Entered empyema 7–21 Cholecystostomy 7–24 Bled 7–28 Myocardial infarction
Stopped	Stopped	—	—	—	Lived 4 unit transfusion
Decreased	Decreased	—	Hours—few Acute ulcers Gastrectomy	—	Lived Could not catheterize L. gastric
Continued	Continued	P & P 43% Fibrinogen 111 Platelets 61,000	1½ hours Superficial gastric & duodenal ulcers V & P ligation bleeding areas	—	Lived Combined hematologic deficits not corrected until in surgery 12 units—2 fresh
Gastric stopped	Massive bleeding from rectum	—	—	—	Died within 24 hours Aorto duodenal fistula unrecognized Exsanguinated
Slowed & Intermittent	Stopped	P & P 70%	—	—	Lived Gastroscopy—superficial ulcers 7 unit transfusion
Slowed	Slowed stopped	—	—	Bled from Rt. Femoral catheter Replaced through left femoral	Died 11–22–71 Cholecystostomy 11–5–71 Infused 11–18–71 Cholecystectomy and C.D. exploration 11–21–71 (No obstruction identified) Renal shutdown Continued sepsis 6 units transfusion 3 platelet packs Expired 5-4-71
Stopped	Stopped Rebled	Platelets 36,000	3 hours Shallow antral ulcers Vagotomy & gastrectomy	Respiratory insufficiency Bleeding uncontrolled at surgery until platelet count 100,000	Autopsy: Esophageal & gastric erosion Extramedullary hematopoesis Bronchopneumonia 12 units bank blood 12 units fresh blood
Stopped	Stopped	—	4 hours Jejunal ulcer Superficial gastritis Vagotomy & gastrectomy	Progressive jaundice Anuria Progressive anoxia	Died 9–7–70 Liver failure Pyelonephritis with renal failure Pseudomonas pneumonia Syphilitis aneurysm 12 units transfused
Stopped	Stopped	LDH 1325	—	Disseminated intravascular coagulation Stopped with Dextran 70	Died 5–17–71 Colectomy 4–28–71 Autopsy: Healed myocardial infarction Squamous carcinoma mouth Bacterial endocarditis Renal infarcts

TABLE 4.—*Continued*

Case No.	Age Sex	Angio Diagnosis	Other Major Diagnosis	Site*	Drug*	Dose	Duration
38	50 M	Gastritis Varices	Alcoholism acute chronic COPD Sinusitis	G.D.	P	.25 μ min	4 hours
			Cirrhosis varices ascites Pneumonia	S.M.	P	.25 μ min	5 hours
39	81 M	Gastritis	ASHD Rupture diaphragm viscera in thorax Chronic obstructive pulmonary dis.	C	E	12 mcg min	20 min
40	50 F	Ulcers Gastritis	Polycystic dis. Renal transplant Immunosuppressed	C	E	20 mcg. min	20 min
					P	.25 μ min	30 min
					Platelets & E	4 μ 20 mcg min	3 hours
41	88 F	Gastritis	ASHD & HCVD atrial flutter pleural effusions Uremic Chr. brain syndrome	C		10 mcg min	5 infusions 10–15 min
42	40 M	Ulcers Varices	Cholecystitis E. coli septicemia	C	E	11–12–70 15 mcg min	40 min
			Cirrhosis varices ascites	S.M.	P		4 hours

Site*: L.G. = L. gastric; G.D. = gastroduodenal; H = hepatic; C = celiac axis; S.M. = superior mesenteric
Drug*: E = epinephrine; P = pitressin

more unusual problems as, for example, intestinal ulcers (Cases 25 & 26) the same is true. Patients massively bleeding from colonic diverticuli are usually elderly which magnifies the risks of operation.

Superficial Ulceration

In the 16 patients who bled from gastritis and/or stress ulcers, there were five failures. In one patient (Case 6), the bleeding from stress ulcers was stopped by angiographic criteria. Clinically, he continued to bleed per rectum. He died within 24 hours and on postmortem examination was found to have bled from an unrecognized aorto-duodenal fistula. He was the only diagnostic failure and may have been survived with operation if correctly diagnosed. One patient (Case 27) developed a hematoma around the catheter site and infusion was stopped after 30 minutes. She rebled and surgical intervention stopped the bleeding. In patient 4, the left gastric artery where the bleeding was originating could not be catheterized for technical reasons. The infusion was performed through the celiac artery and even though the bleeding markedly diminished, the patient required surgical intervention to stop the hemorrhage. Two patients (Cases 30, 34) had unrecognized clotting deficiencies (inadequate platelets and fibrinogen level). Infusion failed in both. They continued to bleed during operation until their defects were corrected, then bleeding stopped. Patient 40, even though eventually controlled with the infusion, rebled until his hypertension was controlled with Apresoline. The latter three patients, as well as previously mentioned Cases 19 and 20, may have stopped bleeding without other treatment if their clotting mechanism had been restored to normal. This trap should be avoided in any bleeding patient. In this last group of patients, we probably influenced the survival of four patients with infusional treatment. Nine patients even-

TABLE 4.—*Continued*

Follow-up			Surgery Time Findings		
Angio	Clinical	Hematologic	Procedure	Complications	Mortality & Notes
Stopped	Stopped Rebled Stopped 2nd Infusion	P & P 60%	—	—	Lived 13 units blood
Stopped	Stopped	—	—	Diaphragm repair 11–30–60 Bled 10 days P.O. Azotemia 91 Jaundice Progressive anoxia	Died 12–6–70 Extensive broncopneumonia
8–24–70 Bleeding 8–26–70 Stopped Stopped	Bleeding Stopped Stopped	P & P 43% PTT 75 sec TT 34 sec Platelets	8–25–70 Superficial ulcers oversewn sewn	Pneumonia Rebled 8–26–70 Rebled 8–27–70 Uremic Dialyzed	Died 8–31–71 Transplanted Pseudomonas lung abscesses HCVD Superficial ulcers: stomach small bowel, large bowel
Decreased each infusion	Decreased Stopped bleeding when hypertension controlled Apresoline	—	—	M.I.	Died 13 days after infusion Myocardial infarction Rebled 4–4–70 (not transfused)
Decreased	Decreased Stopped	P & P 40% Platelets 40,000 Decreased Fibrinogen	—	Cholecystectomy 10–26–70 Drained ascites Peritonitis 11–11–70 Clostridium Septicemia Necrotic sigmoid resected Upper G.I. bleeding 11–11–70 3 hrs. P.O. Liver & renal failure 11–16–70	Died 11–19–70 Superficial stomach ulcers Cirrhosis, ascites

tually died and their mortality was probably not preventable.

Infusional vasconstrictive therapy can reduce regional blood flow and effect cessation of various types of gastrointestinal hemorrhage by allowing stable clot fortion at the point of bleeding. Vessels capable of constriction and adequate coagulation mechanism are prerequisite for this treatment to have a chance of success.

Summary

1) Angiographic technics have a high degree of diagnostic accuracy in defining the source of gastrointestinal bleeding. In massive bleeding they appear more accurate than either endoscopy or barium contrast studies.

2) Therapeutic arterial infusions of epinephrine and/or pitressin into appropriate regional vessels result in control of bleeding most commonly in diverticular bleeding and least commonly in chronic gastric and duodenal ulcers in elderly patients.

3) In a limited experience longer infusions appear to be more successful in prolonged control of bleeding and in this series did not result in ischemic necrosis of the viscera infused.

4) Initial and laboratory studies in progress suggest that pitressin will be the drug of choice for both arterial bleeding and bleeding from varices.

5) Successful treatment of bleeding appears dependent upon the ability of blood vessels to constrict and upon intact hemostatic mechanisms.

6) Later deaths appear to be due to concomitant disease and appear similar in their patterns to the deaths following surgical procedures.

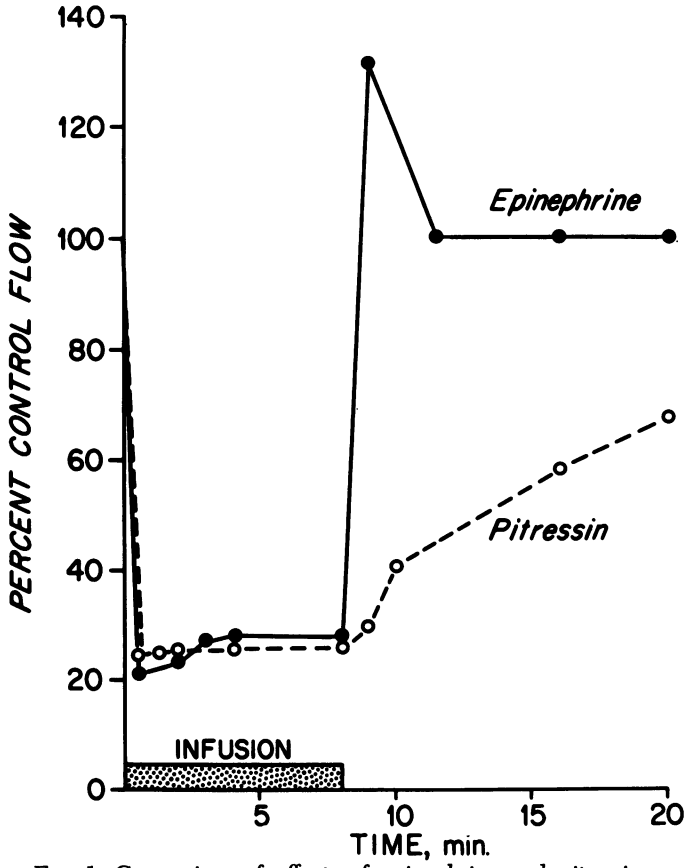

FIG. 1. Comparison of effects of epinephrine and pitressin on superior mesenteric arterial blood flow in the dog. Both agents were infused directly into the superior mesenteric artery. Each point is the mean of experiments in 3 dogs. The epinephrine dose was 3.8 μg per min and was preceded by intramesenteric arterial propranolol, 3 mg. The pitrissen dose was 0.19 U per min. The shaded horizontal bar indicates the duration of infusion.

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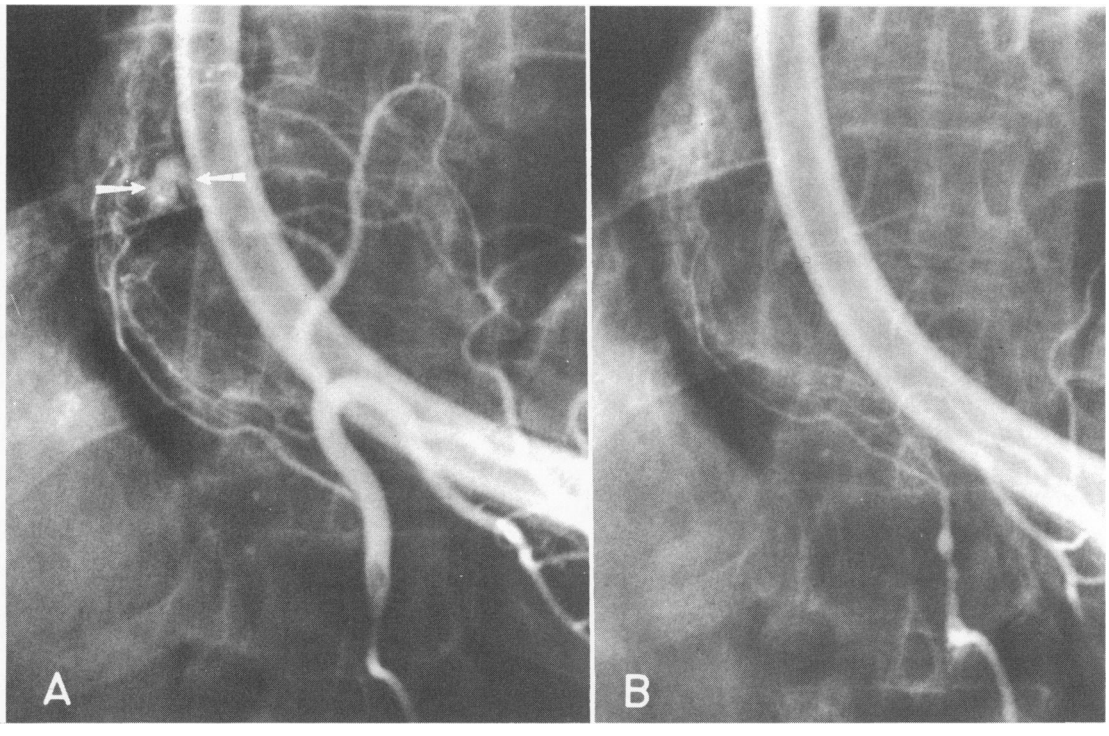

FIG. 2. A 62-year-old man with a hiatal hernia, Mallory-Weiss syndrome, and severe gastrointestinal bleeding. Selective left gastric arteriography. A. Control study demonstrating extravasation of contrast medium on the lateral aspect of the hiatal hernia (arrows). B. Follow-up study after 20-minute infusion of epinephrine at a rate of 10 μg/min., showing extensive constriction of the left gastric artery and its branches with no extravasation.

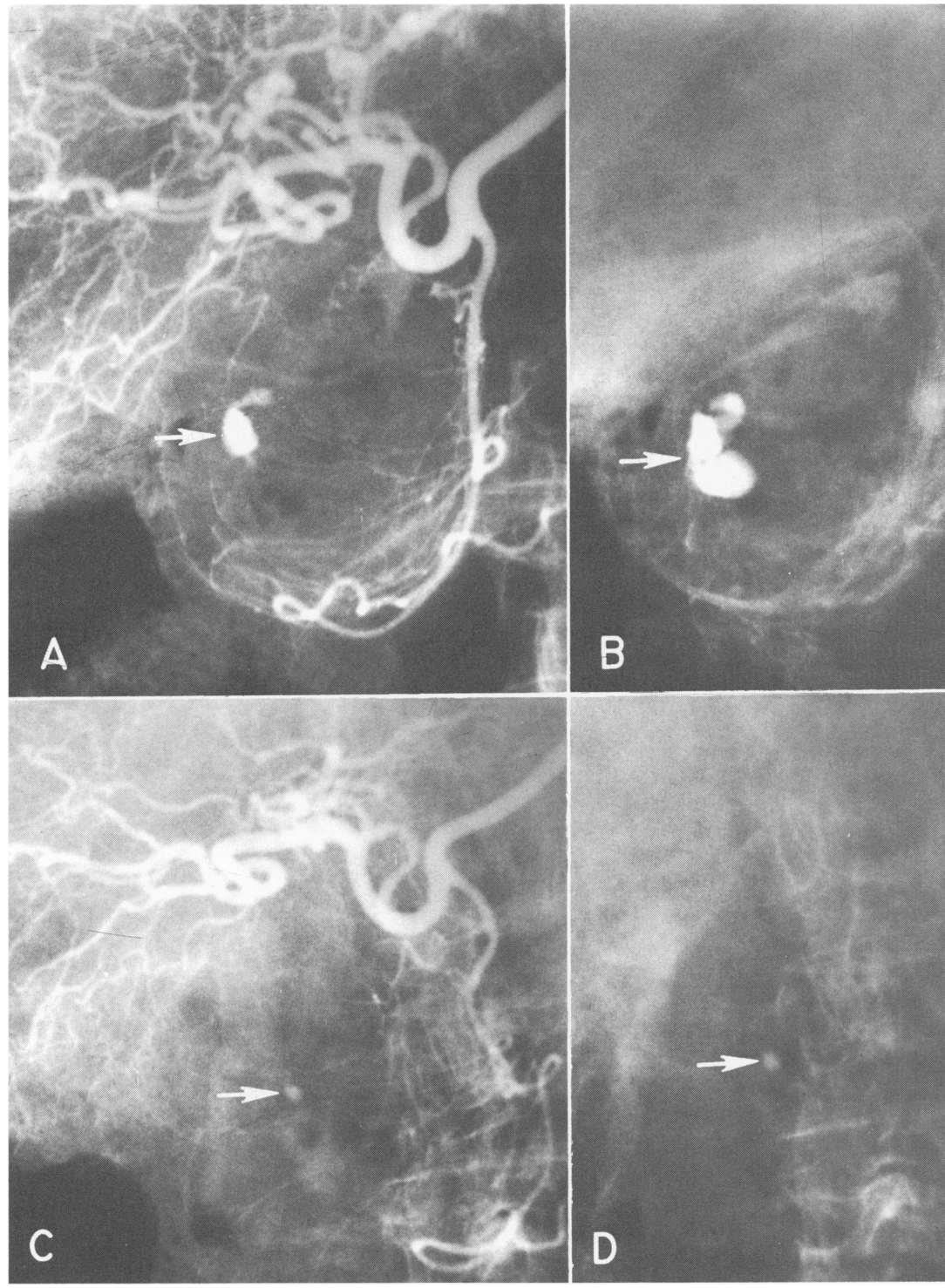

FIG. 3. A 75-year-old man with a duodenal ulcer penetrating into the gallbladder and severe gastrointestinal bleeding. Selective common hepatic arteriography A. and B. Control study. A. Arterial phase showing extravasation of contrast medium into a distended duodenum (arrow). B. Capillary phase demonstrating increased extravasation (arrow). C. and D. Follow-up study after a 20-minute infusion of epinephrine at a rate of 16 μg/min. C. Arterial phase demonstrating moderate constriction of the hepatic and gastroduodenal arteries. Minimal extravasation (arrow). D. Capillary phase showing minimal extravasation (arrow).

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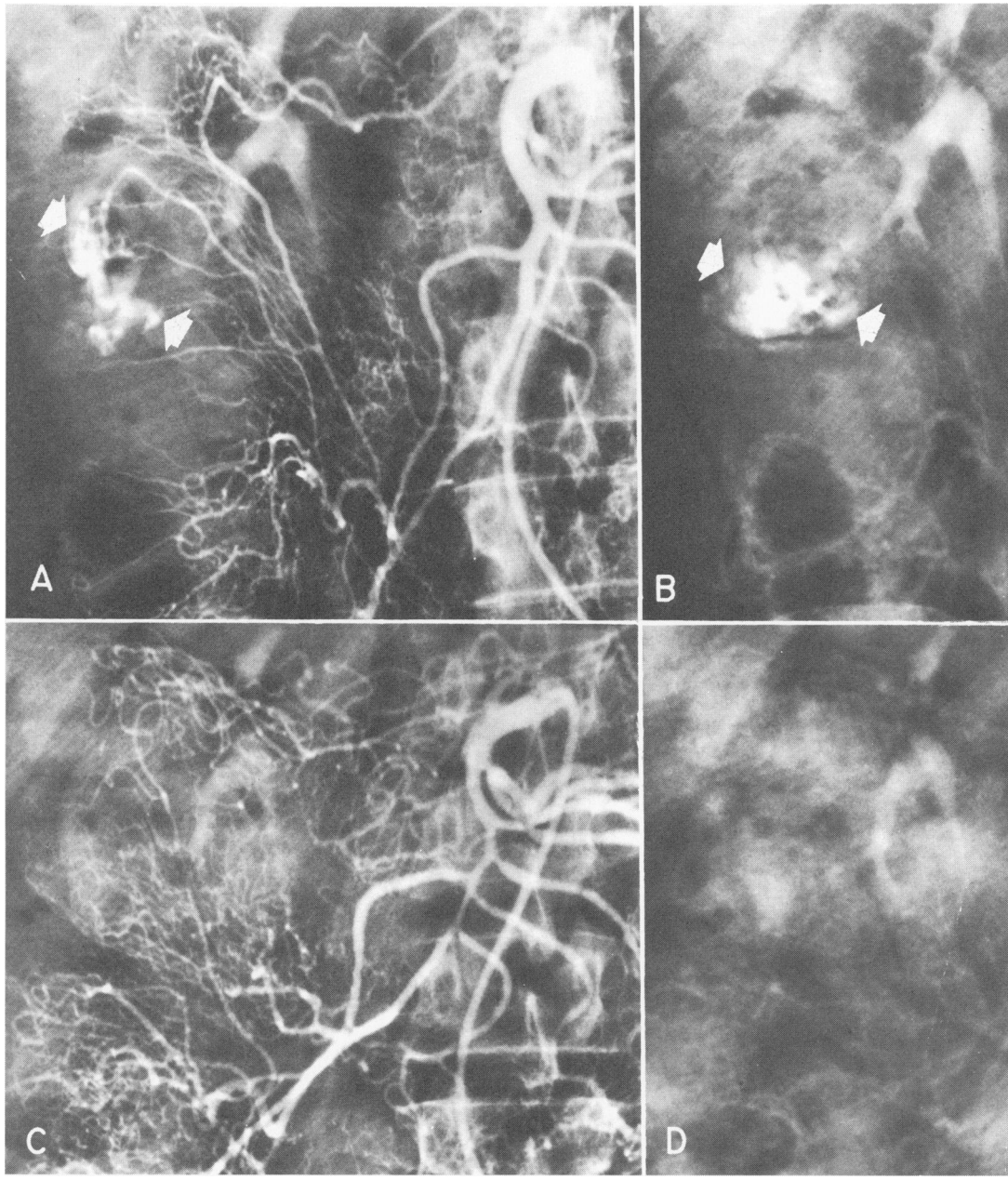

FIG. 4. A. 74-year-old with bleeding diverticulum in the ascending colon. Selective superior mesenteric arteriography. A. and B. Control Study. A. Arterial phase showing extravasation of contrast medium into the colic lumen (arrows). B. Capillary phase demonstrating persistent extravasation of contrast medium (arrows). C. and D. Follow-up studies after 30 minutes infusion of vasopressin at a rate of 0.3 unit/min. C. Arterial phase demonstrating constriction of peripheral branches of colic arteries and no extravasation. D. Capillary phase without any extravasation of contrast medium.

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Discussion

Dr. David B. Hinshaw (Loma Linda): This type of work is predicated on the ready availability of extremely competent angiographers who are interested in working closely with surgeons. In our experience the benefits of "super" selective visceral angiography in acute gastrointestinal bleeding come under three headings. First, it has been extremely helpful in the diagnosis and localization of obscure gastrointestinal bleeding. Second, the precise localization of bleeding points as a guide to the surgeon—for example, to differentiate between bleeding from a peptic ulcer and bleeding esophageal varices in the same patient—or perhaps in localizing a specific site of hemorrhage in the colon. Third, there is an opportunity to control the acute bleeding by the local infusion of vasoconstrictive drugs.

The control of acute bleeding with the localized vasoconstrictive drugs (usually Pitressin) has been especially useful in very poor risk patients, some of whom have been completely controlled and others who have been controlled sufficiently long to improve their chances of successful operative treatment. Along with the authors we, of course, have had our failures.

This angiogram (slide) shows a major bleeding point in the cecum due apparently to a superficial ulceration. In this instance the bleeding was completely and permanently controlled by a localized infusion of Pitressin allowing this elderly poor risk patient to leave the hospital without surgery. In our experience the ability to control active bleeding by this method in the colon has been relatively more effective than the control of bleeding from deep peptic ulceration.

We agree with the authors that angiography in the diagnosis and treatment of acute gastrointestinal bleeding deserves wider and thorough study.

Dr. Leslie Wise (St. Louis): I would also like to congratulate Dr. Brant on his results. Our experience is similar to his, except for the diagnostic accuracy rate.

In our preliminary survey with diagnostic selective angiography of acute gastrointestinal bleeding, we have analyzed 68 cases. Thirty-four of these were positive, thus our yield was 50%. I think we are in a somewhat similar position as operating for acute appendicitis. If we wait until general peritonitis supravenes our diagnostic accuracy rate will be 100%. But if we operate earlier, as most of us do, our diagnostic accuracy will be considerably less.

Six of the studies which were negative for bleeding, however, demonstrated other abnormalities: two demonstrated the typical changes of cirrhosis of the liver; one showed esophageal varices; one demonstrated a large gastric tumor with metastases to the liver; another one showed the typical hyperemia and small vessel tortuosity of the colon, seen in ulcerative colitis; and finally one demonstrated narrowing of the gastroduodenal and pancreatico duodenal arteries, which was subsequently found to be due to a duodenal ulcer.

There were no serious complications directly attributable to the arteriography.

Arteriography was of value even in some cases of known duodenal ulcers and gastric ulcers. In some of these cases the bleeding was not coming from the main ulcer but from a bleeder high up on the lesser curve near the gastroesophageal junction.

With colonic lesions its value is enormous. Here again in some cases the bleeding was not coming from the obvious lesion (such as sigmoid diverticulitis) but from a bleeder in an apparently normal looking colon.

The average time for the performance of the complete arteriogram was less than one hour. We feel that selective arteriography is an extremely valuable tool in the diagnosis of acute gastrointestinal bleeding.

Dr. William S. Blakemore (Philadelphia): About 10 years ago we considered new approaches to the problems associated with gastrointestinal bleeding because of the high mortality for emergency operative procedures and the concomitant lack of diagnostic procedures. Acquainted with some of the information on organ catheterization from Scandinavian investigators, Dr. M. Nusbaum and Dr. S. Baum worked in the laboratory, and after early clinical experience now we can see several distinct areas that are being studied.

One area is that of diagnostic procedure. When the technical details are satisfactory and the bleeding of a patient cannot be demonstrated radiographically, we have confidence that the patient does not have arterial bleeding at the time of the study. Many details regarding other diagnostic uses have been discussed in earlier publications.

For the problems related to treatment of arterial bleeding, we use surgical pituitrin. Dr. Nusbaum worked in the laboratory with various vasoconstrictive substances, showing the site of vasconstriction within the vascular system of the gastrointestinal tract was different with surgical pituitrin and catecholamines. The portal venous bed showed less constriction with the former and arterial constriction with both and did not show tachyphylaxis with pituitrin.

There are several precautions that should be documented. A survey film after the institution of pituitrin or one of the vasoactive substances is required to determine the response in that patient. The dosage is then varied to obtain the desired degree of arterial constriction. In more than 50 patients, we have had only one who did not respond to infusion for variceal bleeding. That patient, with incresed dosage, did not show arterial constriction. In patients with arterial bleeding, the percentage of patients who stopped bleeding has not been as high. The main cause of failure has been the technical failures related to catheterizing the selected vessels. While it is not required to have this procedure done by a radiologist, experience by the man who performs it is required. He should give thought to the procedure beforehand and he should have certain equipment available.

Television video and video tape replay are very helpful as are magnification technics developed by Dr. Baum, who is now at the Massachusetts General Hospital. We think the pituitrin should be continued for 24 to 48 hours after bleeding has been controlled because of the incidence of recurrent bleeding which is a greater risk to the patient than properly monitored infusion for this extended period. The catheter should not be placed in or near the hepatic artery. The effects of long-term infusion on the liver are not known, but we suspect it might cause some damage. We do believe that you can give it safely in to the mesenteric arteries to the other organs, but it must be monitored by angiograms since excess vasoconstriction to the bowel may give you necrosis.