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GASTROINTESTINAL BLEEDING

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Management of gastrointestinal (GI) bleeding is straightforward and logical. The patient must be stabilized, the bleeding stopped, and therapy begun with the hope that further episodes can be prevented. Important advances have been made in terms of resuscitation and supportive measures. Intensive care units are employed in most hospitals, blood components are readily available for more efficient transfusion therapy, and sophisticated patient monitoring devices are widely used. Such advances have improved the likelihood that elderly patients or those with serious underlying illnesses will survive a bleeding episode. [1] New measures to stop bleeding and prevent rebleeding have not been as successful.

Most patients cease bleeding spontaneously. For those who do not, interventional measures are often invasive and not always effective; mortality remains disproportionately high in these patients. Furthermore, recurrent bleeding during the first few days after hospitalization occurs frequently and carries with it increased mortality. If mortality from GI bleeding is to be reduced, safer, more effective means of stopping severe bleeding must be developed and recurrent bleeding must be prevented. These goals are especially important in patients with bleeding esophageal varices. However, even if new modalities are proven effective, they cannot be applied unless the patient has been recognized early-on to have had a bleeding episode, has been accurately assessed as to the severity of bleeding, and has been vigorously and promptly resuscitated. These aspects remain the cornerstone of managing GI bleeding and must not be overshadowed by attempts at early diagnosis or worry that therapy for a specific entity is not being carried out.

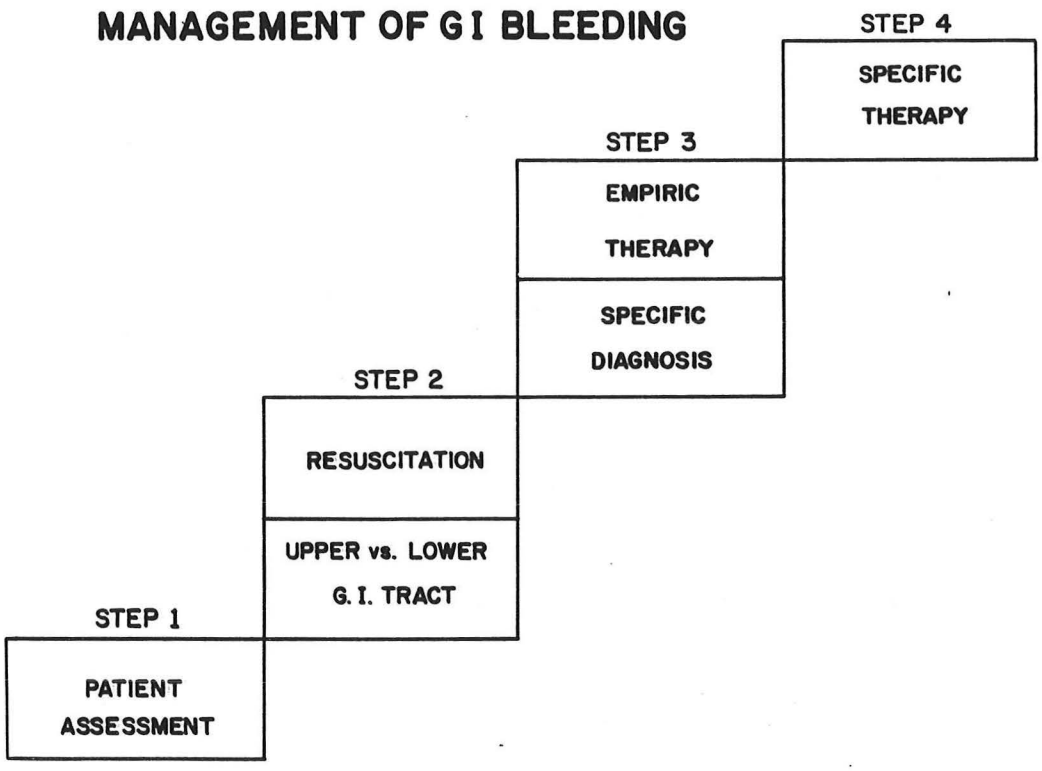
MANNER OF PRESENTATION

Patients manifest blood loss from the GI tract in many ways. *Hematemesis* is bloody vomitus, either fresh and bright-red or older and "coffee-ground" in character. *Melena* is shiny, black, sticky, foul-smelling stool. It results from degradation of blood and must not be confused with the effects of exogenous stool darkeners such as iron, bismuth, or licorice. *Hematochezia* is the passage of bright-red blood from the rectum either in the form of pure blood, blood intermixed with formed stool, or bloody diarrhea. The most common manifestation of GI blood loss is *occult*, detected only by testing the stool with a guaiac reagent. Finally, patients may present without any objective sign of bleeding but rather with *symptoms of blood loss*, such as dizziness, dyspnea, angina pectoris or even shock. Regardless of the presentation, management of the patient proceeds in a step-wise fashion (Figure 1).

ASSESSMENT OF THE PATIENT

When GI bleeding is suspected, rapid assessment of the patient is carried out to gauge the urgency of the situation. Is the bleeding acute or chronic? Is the patient stable or unstable? It is helpful to confirm objectively the presence of GI bleeding with inspection of the stool or nasogastric aspirate, but the first goal is to stabilize the patient. Vital signs are taken, the patient's skin and mucous membranes are inspected for pallor or signs of shock, and blood is sent to the laboratory for complete blood count, clotting studies, and routine chemistry. Blood for typing and cross-matching is sent to the blood bank so if transfusions are necessary, they can be given without delay.

Figure 1.



Presenting Manifestation

Hematemesis, melena, or hematochezia indicate acute episodes of bleeding whereas occult bleeding is generally chronic. Hematemesis results from a combination of large amounts of blood filling the stomach plus the urge to retch which often accompanies vascular collapse. [2] Hematemesis, then, generally indicates a more severe bleeding episode than melena, which occurs when bleeding is slow enough to allow time for degradation of the blood. [3,4] However, there is individual variation, and it would be unwise to assess severity of bleeding solely on this basis. As a general rule, if hematochezia is from an upper GI source, bleeding has been massive (ie., greater than 1000 ml).

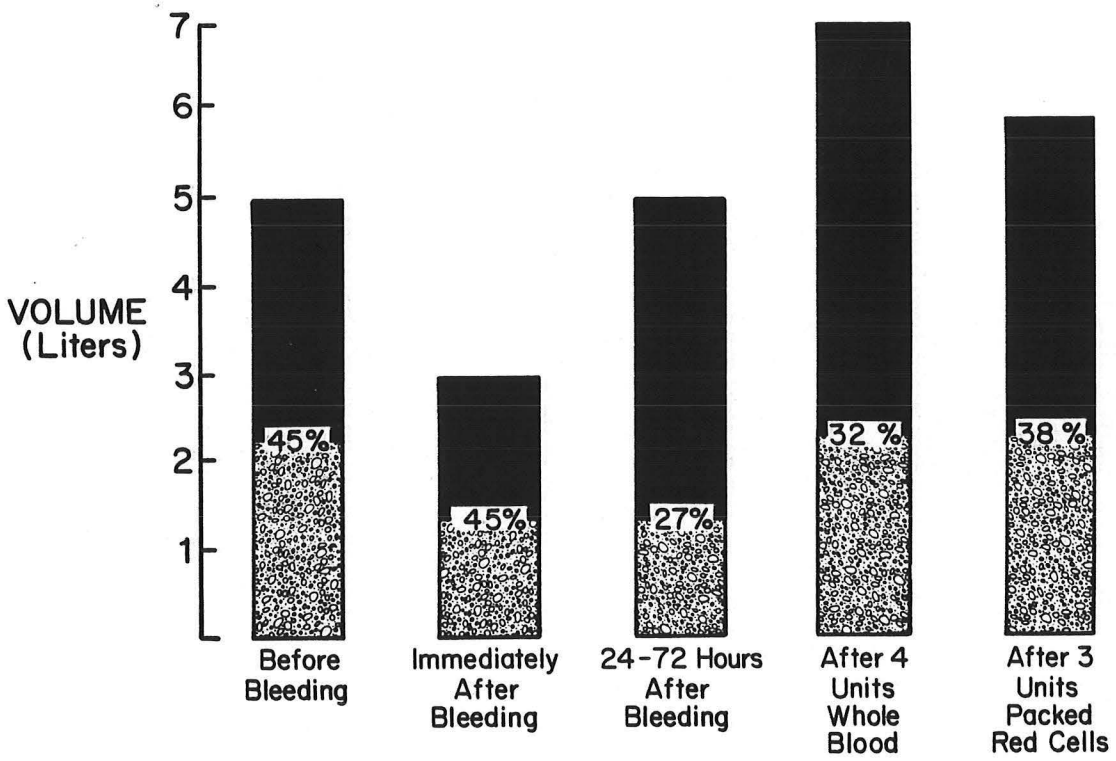
Hematocrit

The hematocrit, often used as an indication of the magnitude of bleeding, reflects the actual amount of blood lost only after acute bleeding episodes.

If a patient bleeds slowly and chronically, many liters of blood may be lost before bone marrow iron stores are depleted and the hematocrit falls. At this time, a peripheral blood smear will usually reveal hypochromic, microcytic red blood cells and the mean corpuscular volume (MCV) of the cells will be low.

If blood loss is acute, the hematocrit will reflect the magnitude of the loss, but not right away. As shown in Figure 2, the hematocrit does not change

Figure 2. Plasma volumes, red blood cell volumes, and hematocrits before bleeding, after two units of blood loss, and after transfusion. Assume a normal hematocrit of 45%. Stippled bars = red blood cell volume; solid bars = plasma volume.



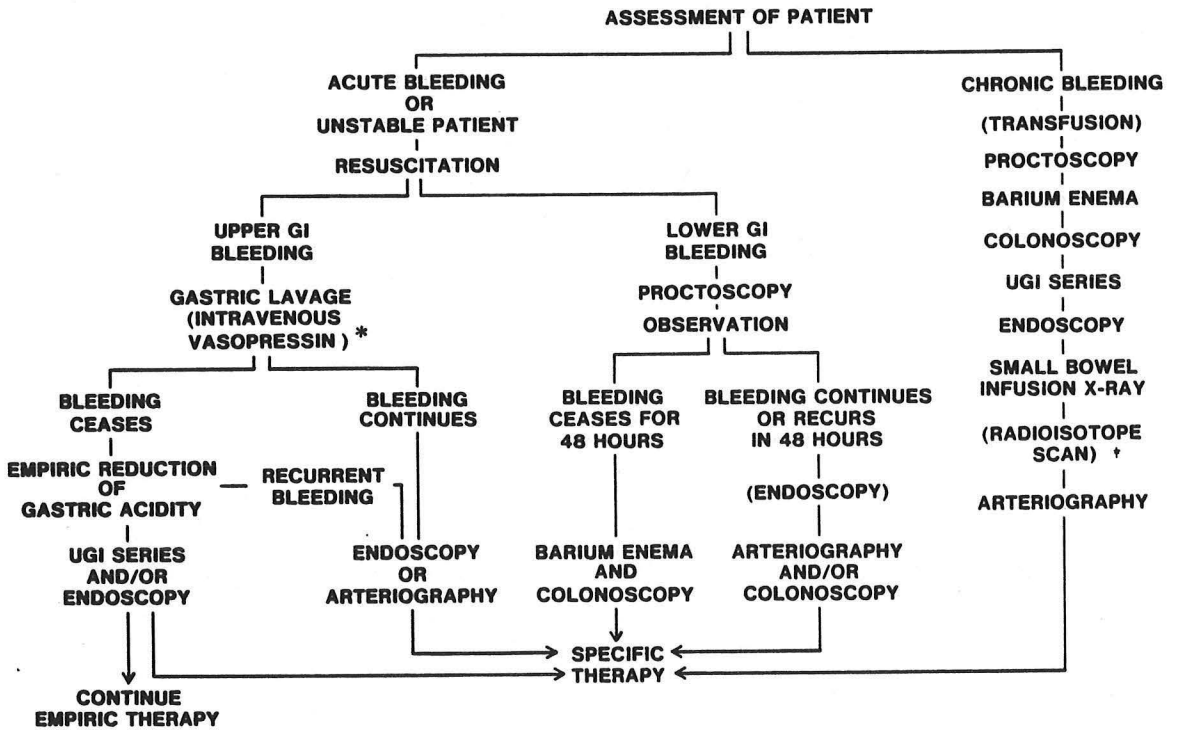
during the first few hours after hemorrhage, since proportionate reductions occur in both plasma and red cell volumes. During this time, caution must be used not to underestimate the severity of bleeding just because the hematocrit is normal. Only as high protein extravascular fluid enters the vascular space to restore volume does the hematocrit begin to fall. This process begins shortly after bleeding occurs but is not complete until total blood volume is restored, often some 24 to 72 hours later. [2] At this point, plasma volume is larger than normal and the hematocrit is at its lowest point. The MCV will be

normal unless there has been prior chronic blood loss. This sequence is modified by administration of exogenous fluids or blood and is not as pronounced in dehydrated patients who have less extravascular fluid to mobilize.

Blood Pressure and Heart Rate

Careful attention to vital signs is the best way to judge a patient's stability, regardless of the hematocrit. The blood pressure and heart rate depend upon the amount of blood loss, the acuteness of blood loss, and the extent of cardiac and vascular compensation. Early-on, or after partial compensation, the only physical finding may be *postural hypotension*. In this instance, blood pressure is maintained if the patient is recumbent but falls when the patient sits up. With greater losses, *tachycardia* and *vasoconstriction* ensue to compensate and finally *recumbent hypotension* occurs. At this point, vascular collapse has occurred and the patient is "shocky" (ie., pale to ashen gray, sweating, distressed). [2] In some patients a *vasovagal reaction* occurs with bradycardia, vasodilatation, and profound constitutional symptoms. [2,5] The individual patient's ability to manifest any or all of these findings depends on cardiac function, vascular integrity, state of hydration, and whether or not the autonomic nervous system is intact. As a rule, a heart rate over 120 beats/minute, a systolic blood pressure under 100 mm of mercury, or a postural drop in blood pressure of 10-15 mm of mercury reflect a blood loss of 1000 ml or more.

Figure 3. Algorithm of management after assessment of the patient. * Patients with cirrhosis; + Younger patients.



Management After Assessment

Figure 3 is an algorithm of management based upon the results of patient assessment. Remember that this is a general approach; variations will occur with individual patients. Stable patients with chronic bleeding are evaluated electively while those with acute bleeding or an unstable condition must immediately be resuscitated.

RESUSCITATION

Patients who have had important acute bleeding or who are in an unstable condition should be admitted to an intensive care unit. Venous access is achieved using large-bore cannulas and fluids are started. Normal saline or lactated Ringer's solution should be infused as rapidly as the patient's cardiopulmonary system will allow; if necessary, attention to central venous or pulmonary capillary wedge pressures will prevent overly-rapid fluid administration in fragile patients. The goal of fluid therapy is to improve quickly the circulation of remaining red blood cells; administration of supplemental oxygen by nasal cannula or face mask permits optimal red cell saturation. Vital signs, urine output, and electrocardiogram are monitored frequently. A flow sheet which documents resuscitative measures and the patient's responses to them is helpful.

When to Transfuse

There are no hard and fast rules to tell a physician when to transfuse a patient with GI bleeding. Common sense dictates that patients who continue to bleed despite therapy, who have very low hematocrits (less than 25 percent) or who have symptoms related to poor oxygenation should be transfused. For asymptomatic, stable patients with hematocrits between 25 and 30 percent, other factors must be considered. Is the hematocrit likely to drop further as vascular repletion occurs? From what hematocrit level could the patient withstand a recurrent episode of bleeding? Is bleeding acute (more likely to need transfusion) or chronic (less likely to warrant transfusion)? If transfusions are deemed unnecessary, iron supplements should be instituted as soon as possible.

What to Transfuse

Blood is transfused to: 1)improve oxygenation (with red blood cells); and 2) improve coagulation (with plasma and platelets). The relative necessity of fulfilling these goals varies among patients and determines the type of blood product(s) transfused. For example, patients who are actively bleeding have both needs and should be given whole blood. Patients who have ceased bleeding

require predominately red blood cells and should receive packed red blood cells. This not only spares the resources of blood banks but, as shown in Figure 2, reduces the volume of fluid transfused. This is especially important in patients with marginal cardiac or renal function. Fresh frozen plasma should be administered routinely with every fourth to sixth unit of packed red cells. Although patients with cirrhosis also respond well to packed red blood cells they often have increased requirements for plasma clotting factors and should receive fresh frozen plasma every second or third unit. [6] Whenever packed red cells are given, platelet packs are necessary every four to six units.

How Much To Transfuse

Patients should receive blood until their condition stabilizes, bleeding ceases, and enough red blood cells are circulating to provide adequate oxygenation. A hematocrit of 30 percent is a reasonable goal in most patients and provides a buffer if recurrent bleeding ensues. Remember that plasma volume is often overexpanded after GI bleeding and the hematocrit shortly after transfusion may underestimate the oxygen carrying capacity of blood (Figure 2).

UPPER VERSUS LOWER GI TRACT BLEEDING

As resuscitation is being carried out, the source of bleeding must be localized to the upper or lower GI tract to direct further management (Figure 3). Hematemesis, either alone or in combination with other manifestations, indicates an upper GI (above the Ligament of Treitz) source of bleeding. Melena occurs if enough hemoglobin in the GI tract is oxidized to hematin or other hemichromes to blacken the stool. [7] At least 100 to 200 ml of blood is needed. [8] Since this reaction appears to be dependent upon the time blood remains in the intestine (and perhaps contact with gastric acid), most patients with melena have bled from an upper GI source. [4,8] Bleeding colonic lesions may occasionally produce melena, [4,7,9] but only if three conditions are met. First, there must be enough blood degraded to blacken the stool. Second, bleeding must not be too brisk or hematochezia will ensue. Third, colonic motility must be sluggish to allow enough time for degradation to occur. Most colon lesions either bleed in such small amounts that only occult blood is present in stool or so briskly that hematochezia occurs. Hematochezia usually represents a lower GI source of bleeding although an upper GI lesion may occasionally bleed so briskly that blood does not remain in the bowel long enough to become melena. Lesions of the small bowel may present as either hematochezia or melena, although small bowel lesions are unusual sources of GI bleeding.

Whenever question arises as to the location of bleeding, a nasogastric tube should be placed. A bloody aspirate confirms an upper GI source, while a negative aspirate virtually excludes active upper GI bleeding. [10] Interpretation (by guaiac reaction) of aspirates that are not grossly bloody should be cautious since both false-positive and false-negative results may occur. [11] Occasionally, a postpyloric upper GI lesion will bleed (even massively) without reflux into the stomach and the aspirate will be negative. Endoscopy is the only sure way of detecting such occurrences, but other findings suggestive of upper GI bleeding include hyperactive bowel sounds and elevation of the blood urea nitrogen (BUN) above 30 to 40 mg/dl. Such rises in the BUN occur after major upper GI bleeding episodes (1000 ml or more) [12] and are the result of volume depletion plus absorbed blood proteins. [13] Either factor alone will

not result in elevation of the BUN to this degree. A summary of differentiating features of upper and lower GI bleeding is shown in Table 1.

Table 1. Differentiating features of upper GI and lower GI bleeding.

	UPPER GI	LOWER GI
Presenting Manifestation	Hematemesis or Melena	Hematochezia
Nasogastric Aspirate	Positive	Negative
Blood Urea Nitrogen	Elevated	Normal
Bowel Sounds	Hyperactive	Normal

ACUTE UPPER GI BLEEDING

It may be estimated that at least a quarter-million people are admitted with acute upper GI bleeding each year in the United States [14] and, with few exceptions, [15,16] overall mortality figures from current series are little different from those 40 years ago. [1,17-19] Despite modern diagnostic and therapeutic modalities, about 10 percent of patients with upper GI bleeding still die. Hidden in this average figure, however, are several pertinent observations:

1. Mortality in patients over 60 y/o has been well recognized to be higher by several fold than in younger patients. [17,19-21] Since the proportion of bleeding patients who are over 60 y/o has increased during the last 40 years from about 30 percent to about 50 percent, [1,18] it might have been expected that overall mortality would also have risen. One reason that it has not risen, but instead has remained constant, may be that mortality in older patients has in fact decreased. [19]
2. Patients who bleed from esophageal varices account for a disproportionate number of deaths (Table 2). While mortality with bleeding duodenal ulcer is

Table 2. Overall mortality, incidence of rebleeding, and increased mortality with rebleeding for the most common causes of upper GI bleeding.

Lesion	Overall mortality[1]	Incidence of rebleeding[2]	Increased Mortality with rebleeding[3]
Duodenal Ulcer	1-7%	12-30%	4-6X
Gastric Ulcer	7-16%	25-48%	3-6X
Esophageal Varices	22-63%	56-70%	2-4X

[1] References 1, 15-17, 19, 23

[2] References 22, 23, 25

[3] References 22, 23, 26

between 1 and 7 percent and with gastric ulcer between 7 and 16 percent, mortality following variceal bleeding ranges from 22 to 63 percent, with most series reporting over 40 percent. Thus, series with a low proportion of cirrhotic patients tend to have lower overall mortality. For example, Meulengracht reported 35 years ago that of 1031 patients with bleeding "peptic ulcer", only 26 (2.5 percent) died. [24]

3. A major proportion of deaths from any given lesion occurs in those patients who continue bleeding after admission to hospital [17] or who stop bleeding and then rebleed during the first 48 hours (Table 2). [23,25] While overall mortality in patients who cease bleeding and do not rebleed is from two to eight percent, mortality after rebleeding is from 10 to 22 percent. [17,20,22,23] One reason that continued bleeding or rebleeding carries with it such a disproportionately high mortality is that radical therapy, such as urgent surgery, is often required to stop the bleeding. Mortality after urgent surgery is approximately three times greater than that with non-surgical or elective surgical therapy. [17,26,28]

Thus, the goals of therapy after resuscitation in patients with upper GI bleeding are clear. First, bleeding must be stopped quickly without resorting to urgent surgery or other invasive therapy. Second, rebleeding (especially from esophageal varices) must be prevented. Measures designed to achieve these goals may be either empiric or specific. Empiric therapy is administered without a diagnosis in hand and must therefore be relatively safe and not require special expertise. Specific therapy, on the other hand, is usually more invasive or requires special skills; a specific diagnosis is needed first.

Empiric Therapy to Stop Active Bleeding

Gastric lavage- Rinsing the bleeding stomach with iced saline is a time-honored empiric technique, the rationale for which is reduction of gastric blood flow. [29] While there are no controlled data proving its effectiveness, gastric lavage is associated with at least temporary cessation of bleeding in over 90 percent of patients, regardless of diagnosis. Even if it were of no help in controlling bleeding, lavage gives a good indication of the rapidity of bleeding and serves to cleanse the stomach for possible later endoscopy. A large bore (34-36 French) orogastric tube is placed after removing the smaller diameter nasogastric tube used for localization of bleeding. Aliquots of fluid (500 to 1000 ml) are instilled and then removed by gentle suction and gravity drainage. Iced saline is traditionally used although experimental evidence suggests that room temperature tap water may be as effective. [30-32] Room temperature fluids do not reduce blood flow well but they may impair coagulation less than do cold fluids. [29,30] Lavage is continued until bleeding stops or until it becomes evident that other measures will be necessary. Ten or more liters of fluid may be needed.

Drug Therapy - Most bleeding ceases during lavage. If bleeding does not cease, several pharmacologic agents have been suggested as empiric therapy. *Intragastric levarterenol* (Levophed [R]) (8 mg in 100-250 ml saline) does not reduce gastric blood flow any more than cold lavage alone [29] but has nonetheless been reported as "effective" in controlling on-going bleeding. [33-35] These are uncontrolled studies and do not justify the use of this agent except as a last-ditch effort. *Tranexamic acid*, an antifibrinolytic agent, has undergone two controlled trials with unimpressive results. [36,37] In neither study was survival improved by the drug.

There are at least three reasons why measures to reduce gastric acidity might be effective as empiric therapy in patients with continued bleeding. First, peptic ulcers (believed to be perpetuated by gastric acid) are a frequent cause of upper GI bleeding. Second, pepsin, which promotes platelet disaggregation, [38] is inactivated at high gastric pH. [39,40] Third, there is in-vitro evidence to suggest that blood coagulation is optimal when gastric pH is high. [38] *Antacids* have been studied only in patients bleeding from acute gastritis. [41-43] In one study, low doses of antacid either alone or with modest doses of cimetidine arrested bleeding in only one third of patients. [41] A placebo-treated group was not employed. Antacids in doses sufficient to maintain gastric pH at 7.0 have been reported in another study to stop bleeding in 90 percent of patients with acute gastritis. [42] However, since no control patients were included, there is no proof that this approach is better than a less intensive one or none at all.

Cimetidine has been evaluated against placebo in two series of patients with continuing upper GI bleeding of various causes, and in neither was it successful. [44,45] In one study, bleeding ceased in 75 percent of cimetidine-treated patients compared to 82 percent of placebo-treated patients. [45] It is of interest that cimetidine was significantly less effective than placebo in controlling bleeding from gastric lesions. These two studies employed cimetidine in doses of 1200 mg per day, a dose which may not raise gastric pH to high enough levels to achieve benefit. *Somatostatin*, another drug which reduces gastric acidity, has been reported to be more effective than cimetidine in stopping bleeding from peptic ulcers. [46,47] The studies are small and poorly-controlled. Again, cimetidine was used in doses that may not have reduced gastric acidity to the same extent as somatostatin. It has also been suggested that somatostatin, by lowering portal venous pressure, might be useful in treating esophageal varices. [48] This study was uncontrolled and there is even some doubt whether somatostatin lowers portal pressure. [49]

Vasopressin is a vasoconstrictor agent which is effective in controlling bleeding from esophageal varices. If used intra-arterially, a specific diagnosis should be made first, since arteriography requires special expertise. However, a low-dose constant infusion of vasopressin by vein is equally effective and can be instituted without requiring a skilled angiographer. In patients with evidence of cirrhosis and portal hypertension, it is reasonable to try intravenous vasopressin empirically if bleeding continues. A dose of 0.4 units per minute is given. If bleeding ceases, this dose should be continued for 24 hours, after which it is tapered over the next 48 hours. If bleeding continues, some would increase the dose to as much as 1.5 units per minute, although complications are more likely to occur. Vasopressin should be used with caution in patients with vascular disease, coronary artery disease, or a history of cardiac arrhythmias. Hyponatremia commonly occurs with use of vasopressin by virtue of its antidiuretic hormone effect.

Thus, with the exception of vasopressin for patients with cirrhosis and portal hypertension, there is no good empiric therapy for continuing bleeding beyond gastric lavage. If bleeding continues, more specific (and more invasive) measures will be needed. In this situation, the next step is to make a rapid, specific diagnosis. The majority of patients cease bleeding, however, and immediate diagnosis is not as important. The next step for these patients is to institute empiric measures which might reduce the incidence of rebleeding.

Empiric Therapy To Prevent Recurrent Bleeding

Agents employed to prevent rebleeding have included *cimetidine, antacids*, or a *combination of the two*. Trials performed in the United Kingdom have demonstrated no benefit of various doses of cimetidine, when compared to placebo,

in preventing recurrent bleeding from duodenal ulcer. [50-52] In one study, however, cimetidine was significantly better than placebo in preventing rebleeding from gastric ulcer. [52]

Neither cimetidine (300 mg every six hours) nor hourly antacids alone was better than placebo at preventing rebleeding from a variety of causes in a large United States trial. [45] However, the combination of the two reduced the incidence of rebleeding by one-half compared to placebo. In duodenal lesions specifically, rebleeding occurred in six percent of patients receiving the combination compared to 18 percent with placebo. These data, and those from one other study, [41] suggest that regimens producing intragastric pH levels higher than cimetidine or antacid alone are more effective. At least theoretically, the optimum regimen would be one that sustained gastric pH at 7.4 for 24 hours a day. To achieve this, it may be necessary to administer cimetidine as a constant intravenous infusion at doses up to 100 mg per hour in conjunction with hourly doses of potent liquid antacid by mouth.* Whether this regimen would be safe or more effective clinically is not known.

Diagnostic Approach to Acute Upper GI Bleeding

Patients who continue bleeding despite empiric therapy almost always require a specific diagnosis. Patients who cease bleeding may or may not require a diagnosis depending upon the situation. The following section proceeds under the assumption that a specific diagnosis (Table 3) is desired in a given patient.

Table 3. Causes of GI bleeding

Upper GI	Upper or Lower GI	Lower GI
Duodenal Ulcer	Neoplasms	Hemorrhoids
Gastric Ulcer	- Carcinoma	Anal Fissure
Marginal Ulcer	- Leiomyoma	Diverticulosis
Esophageal Varices	- Sarcoma	Meckel's Diverticulum
Mallory-Weiss	- Hemangioma	Ischemic Bowel Disease
Gastritis	- Lymphoma	Inflammatory Bowel Disease
Esophagitis	- Melanoma	Solitary Colonic Ulcer
Hematobilia	- Polyps	Intussusception
Menetriere's Disease	Arterial-enteric fistulas	
	Vascular Anomalies	
	- Osler-Weber-Rendu	
	- Blue Rubber Bleb Nevus	
	- CRST Syndrome	
	- Arterio-venous malformations	
	- Angiodysplasia (vascular ectasia)	
	Hematologic Disease	
	Elastic Tissue Disorders	
	- Pseudoxanthoma elasticum	
	- Ehlers-Danlos	
	Vasculitis syndromes	
	Amyloidosis	

* Peterson, W.L. Unpublished observations.

History and Physical Examination - As the initial steps of management are being carried out, it is important to take a history and perform a physical examination. While a specific diagnosis can only occasionally be made this way, helpful clues may be obtained. Have there been prior episodes of bleeding? Is there a family history of diseases that cause bleeding? Does the patient have other illnesses that may lead to bleeding, such as cirrhosis, cancer, coagulopathies, connective tissue disorders, or amyloidosis? Has there been prior surgery such as for peptic ulcer or to place arterial bypass grafts? Does the patient drink alcohol to excess or take drugs such as aspirin on a chronic basis? Has there been caustic ingestion? Was the bleeding episode preceded by abdominal pain, dyspepsia, or retching? Has the patient had nosebleeds?

Examination of the skin is potentially the most helpful aspect of the physical examination. Stigmata of cirrhosis, evidence of underlying malignancy (acanthosis nigricans, Kaposi's sarcoma) or hereditary vascular anomalies may be found. Findings with pseudoxanthoma elasticum or Ehlers-Danlos syndrome are diagnostic. Further physical findings include lymphadenopathy or abdominal masses (malignancy); abdominal tenderness (peptic ulcer); and splenomegaly (cirrhosis or splenic vein thrombosis).

Barium X-Rays and Endoscopy - Since the history and physical examination are rarely diagnostic, other techniques are necessary to define the bleeding lesion. With rare exception, [53] endoscopy performed early-on has been reported to diagnose more lesions that standard, single-contrast barium studies of the upper GI tract. [54-57] Analysis of these studies discloses that this benefit is due primarily to greater accuracy with acute mucosal lesions (esophagitis, Mallory-Weiss tears, gastritis). [54,56,58] Furthermore, seeing a lesion on an x-ray does not exclude the possibility that another, unseen, lesion is actually bleeding. Double-contrast barium studies are better than single-contrast x-rays (even to the point of visualizing "active bleeding") but still do not achieve the accuracy rates of endoscopy. [59,62] While the primary site of bleeding can be detected in 80-85 percent of patients with double-contrast radiography, endoscopy will detect 90-95 percent. [60-62] The differences remain in terms of acute mucosal lesions and, in clinical situations, these differences would likely be of little importance since such lesions are usually self-limited. However, barium introduced into the stomach makes investigation soon after with either endoscopy or arteriography difficult. Employment of water soluble, clear contrast agents (such as Gastrografin [R]) to obviate this problem produces x-rays of unsatisfactory quality. Thus, endoscopy is the procedure of choice for patients with continuing bleeding while barium studies, if performed, should be reserved for patients whose bleeding has ceased.

Arteriography - Upper GI bleeding may be so brisk in some patients that endoscopy cannot be performed or a confident diagnosis cannot be made. Selective mesenteric arteriography will localize the source of bleeding (usually from the left gastric artery) in about 75% of patients. [63-65] It is widely accepted that blood loss must be at a rate of 0.5 to 0.6 ml per minute for extravasated dye to be seen on x-ray. [66] Arteriography will be negative if flow rates are less than this or if the patient is bleeding from a venous lesion. Although varices may be seen during the venous phase of an injection, extravasation is rarely noted since, by this time, the dye is too dilute. Another advantage of arteriography is the ability to selectively infuse vasoconstrictor agents as

a means of controlling bleeding. The main disadvantage is the requirement for a readily-available, expert angiographer.

Radioisotopes - Intravenous injection of a radioactive substance and detection of intestinal extravasation by an isotope counter is, theoretically, a nice, non-invasive way to localize active bleeding. Technetium - 99 (Tc-99) sulfur colloid [67] is cleared rapidly from the bloodstream by liver and spleen. This means that bleeding may be detected for only a short time after injection and, because of uptake in the liver and spleen, upper GI lesions are difficult to see. Means of avoiding these difficulties include attaching Tc-99 to albumin, [68] red blood cells, [69] or heat-treated red blood cells. [70] Whether any of these approaches will stand up to clinical evaluation in human subjects remains to be seen. The obvious use would be as a screening test before urgent arteriography. If a bleeding site is not seen, or if intra-arterial vasoconstrictor therapy is not desired, arteriography would not be necessary. Use of this technique for chronic, slow bleeding or intermittent episodes of bleeding does not seem promising with the possible exception of Meckel's diverticulum.

Suggested Overall Diagnostic Approach - Patients who continue to bleed despite empiric therapy should be promptly endoscoped to find the specific lesion for which specific therapy is needed. For example, a patient with bleeding esophageal varices may require balloon tamponade while a patient with a bleeding duodenal ulcer should go to surgery. If endoscopy cannot be performed or if selective vasoconstrictor therapy is required, arteriography is warranted.

The approach to the patient who ceases bleeding is less straightforward but, as with the patient who continues to bleed, often includes routine early endoscopy. The rationale is that making a prompt diagnosis will aid in the patient's management. Several controlled trials involving diverse patient populations suggest that, at least in terms of objective measurements of outcome, this is not the case. [22,55,57,61,71-73] Routine performance of endoscopy does not improve survival, reduce transfusion requirements, or shorten hospital stay. Prior knowledge of the source of bleeding does not improve the outcome of patients who rebleed and, in one study, 12 month follow-up did not disclose a benefit to patients who were routinely endoscoped. [22] There is at least one good explanation for these observations. A diagnosis is only as good as the therapy to which it leads and, for patients who cease bleeding, therapeutic options are limited. If a patient has bled from peptic ulcer, antacids or cimetidine are currently used as therapy; when and if to perform elective surgery is an unsettled issue. If bleeding has been from a Mallory-Weiss tear or gastritis, antacids or cimetidine are, again, the only therapy available. While some physicians choose portal-systemic shunts for patients who have bled from esophageal varices, there is little evidence that overall survival is improved. In summary, there is currently no better, proven therapy for any lesion (if bleeding has ceased) than cimetidine or antacids. Thus, one approach to patients who *cease bleeding* is as follows:

1. Begin empiric therapy with an intensive intravenous cimetidine and oral antacid regimen to raise intragastric pH; continue for three days (the period during which rebleeding is most likely to occur).
2. If rebleeding does not occur, change empiric therapy to standard oral cimetidine or antacid regimens for peptic ulcer and continue four to six weeks.
3. Perform an upper GI barium x-ray, preferably double-contrast. While this is not necessary in every patient, it will reliably detect malignant lesions

(although they are unusual causes of acute upper GI bleeding), will often diagnose other lesions, and is less expensive than endoscopy. If a specific diagnosis is made, empiric ulcer therapy may be continued unchanged, modified, or stopped.

4. Endoscopy should be performed if rebleeding occurs in hospital, if barium x-ray discloses a possible malignancy or gastric ulcer, or if important individual decisions in therapy (such as elective surgery for peptic ulcers or esophageal varices) depend upon a reliable, specific diagnosis. Patients with recurrent episodes of acute bleeding might also be included in this last group.

Several arguments have been raised to this approach, despite the results of controlled clinical trials. [74] First, there are physicians who believe endoscopy should be performed routinely to select-out patients with peptic ulcer in whom there are "stigmata" of recent bleeding (ie., visible vessel or adherent clot). [75-77] These patients may rebleed and require urgent surgery more often than patients without such findings. However, there is no convincing evidence to support routinely sending these patients to early surgery just because they have such lesions. Prophylactic electrocoagulation has been suggested as a means of preventing rebleeding from visible vessels but only a few patients have been studied. [78] Prophylactic argon laser photocoagulation has also been tried with visible vessels; 8 of 19 patients in a laser-treated group experienced further bleeding compared to 8 of 16 control patients (no significant difference). [77] Only when there is a proven approach to patients with "stigmata" will there be reason to look for these lesions.

Second, the incidence of rebleeding with esophageal varices is so high that some physicians have turned to prophylactic endoscopic variceal sclerosis, an old procedure experiencing a rebirth (see page 18). If this approach is taken, patients with liver disease need to be endoscoped to make sure no lesion other than varices is responsible for the bleeding episode and then to have the procedure performed. While this approach may have merit, more data are needed to prove its efficacy and safety.

Finally, some physicians believe that "knowing the diagnosis" has intangible worth. For example, a patient may be better counseled if an accurate diagnosis has been made. It is difficult to refute such an argument and it is unlikely a controlled trial will be done to settle the issue.

Approach to Specific Upper GI Bleeding Lesions

Peptic Ulcers - A duodenal, gastric, or marginal (post-gastrectomy) ulcer is the responsible lesion in 40 to 50 percent of patients with upper GI bleeding. If bleeding continues, strong consideration should be given to early surgical therapy. Similarly, a patient who rebleeds while on medical therapy is generally considered a surgical candidate. If bleeding stops and does not recur, one may select from several ulcer therapeutic agents, including cimetidine and antacids. Other histamine receptor antagonists, such as ranitidine, and new agents such as sucralfate or one of the prostaglandins may also soon be available. The issue of when to recommend elective surgery for patients with bleeding ulcer is unresolved, especially since maintenance cimetidine therapy is now available.

Mortality from bleeding ulcers occurs most often in patients who are elderly, have underlying illnessess, and require urgent surgery. Means of controlling bleeding other than urgent surgery have therefore long been sought. Because of success in using *selective arterial infusion of vasopressin* in acute mucosal lesions (see page 21), this approach has also been tried in acute peptic ulcers. Perhaps because of large, complex vasculature around peptic ulcers, [79,80] intra-arterial vasopressin is rarely effective. [80-82] Another angiographic technique is *embolization* of autologous clot or some foreign

material such as gelfoam into the bleeding artery.[83-87] Although successes have been noted in individual patients, this technique requires much expertise and is associated with frequent complications.[84,86,88,89] While embolization therapy for peptic ulcers may be life-saving in patients who could not survive surgery, it should be used only by skilled angiographers and only when the clinical situation is desperate.[82]

Better candidates for non-operative therapy of bleeding ulcers are those which can be applied endoscopically. Skilled endoscopists are more abundant than skilled angiographers and endoscopic therapy may be safer. Endoscopic modalities may be lumped into two groups - those which do or do not produce heat. Nonthermal methods include spraying *clotting factors*[90] or *cyanoacrylate tissue glues*[91,92] onto a bleeding lesion. Evidence in animals that either will control important bleeding is unimpressive and controlled trials in humans have not been reported.

Thermal methods of endoscopic therapy include the heater probe, laser photocoagulation, and electrocoagulation. The *heater probe* consists of a heater element within a teflon-coated aluminum cylinder.[93] When applied endoscopically to experimental bleeding lesions in dogs, the hot cylinder stops the bleeding but produces deep tissue injury. *Laser photocoagulation* occurs when heat is generated by interaction of laser light and tissue. Two sources of laser, argon and neodymium-YAG (Nd-YAG), have been tested in animals with good success.[94-100] Tissue injury is less than with the heater probe but laser, especially Nd-YAG, still possesses the potential of perforating the bowel if not used carefully. Early controlled trials of endoscopically delivered laser in human subjects suggest that when used properly, both argon and Nd:YAG laser are safe and will stop bleeding.[77,101] Unfortunately, laser is expensive to purchase and to maintain and cannot be moved to the patient. The latter is a disadvantage for sick patients who ideally should not be moved from an intensive care unit.

A potentially more practical endoscopic technique is *electrocoagulation.* The equipment is less expensive, portable, and more easily maintained. In animal models, various types of electrodes (monopolar, bipolar, multipolar) each stop bleeding;[102,103] bipolar or multipolar appear to be the safer electrodes and are as effective as argon laser.[103,104] Monopolar electrodes have been used in humans with apparent success, but these have all been uncontrolled studies.[78,105,106] Controlled trials showing safety and efficacy are needed before electrocoagulation is widely used.

Esophageal Varices - Management of patients with bleeding esophageal varices * remains the largest stumbling block to reducing overall mortality from upper GI bleeding. Prognosis for these patients is dreadful. A third or more will die during hospitalization,[22,107,108] at least a third will rebleed within six weeks,[108] and no more than a third will survive beyond one year (Figure 4).[108,109] Series with better results may reflect inclusion of fewer poor-risk patients[110] or perhaps isolated success with one of several means of therapy. It is no wonder that there have been proposed a number of therapeutic techniques whose goals are to improve this outlook; the fact that a new one surfaces each decade implies that none has been successful.

What factors determine whether esophageal varices will develop? Will bleed? Although there must be a critical portal blood pressure at which esophageal veins begin to dilate, there is no relationship between portal pressure and either the size of varices or their propensity to rupture and bleed.[111,112] There is, however, a correlation between the size of varices and the risk of bleeding.[112]

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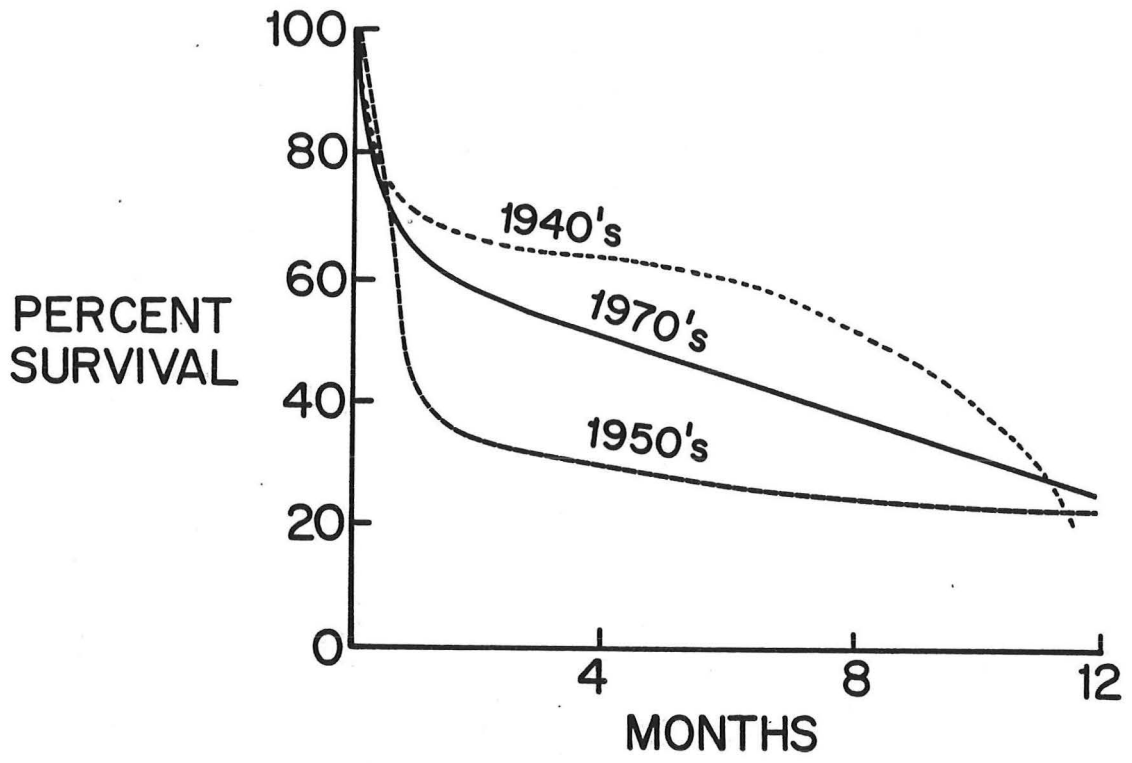
* For purposes of this discussion, gastric varices (which also pose important problems) will be lumped with esophageal varices.

Figure 4. Survival after variceal bleeding in three different decades (From Ref. 108).



This implies that esophageal veins under pressure stretch gradually with time. When they reach a large size (over 5 mm in diameter), they are more likely to burst. This follows LaPlace's law of cylinders (tension on the wall is proportional to pressure and radius); larger cylinders (or veins) must have stronger walls to withstand a given pressure. [113] While transient large increases in portal pressure (as a result of blood volume overload [114-116]) may play a contributing role to variceal bleeding, mucosal inflammation from gastroesophageal reflux appears to be unimportant. [113,117]

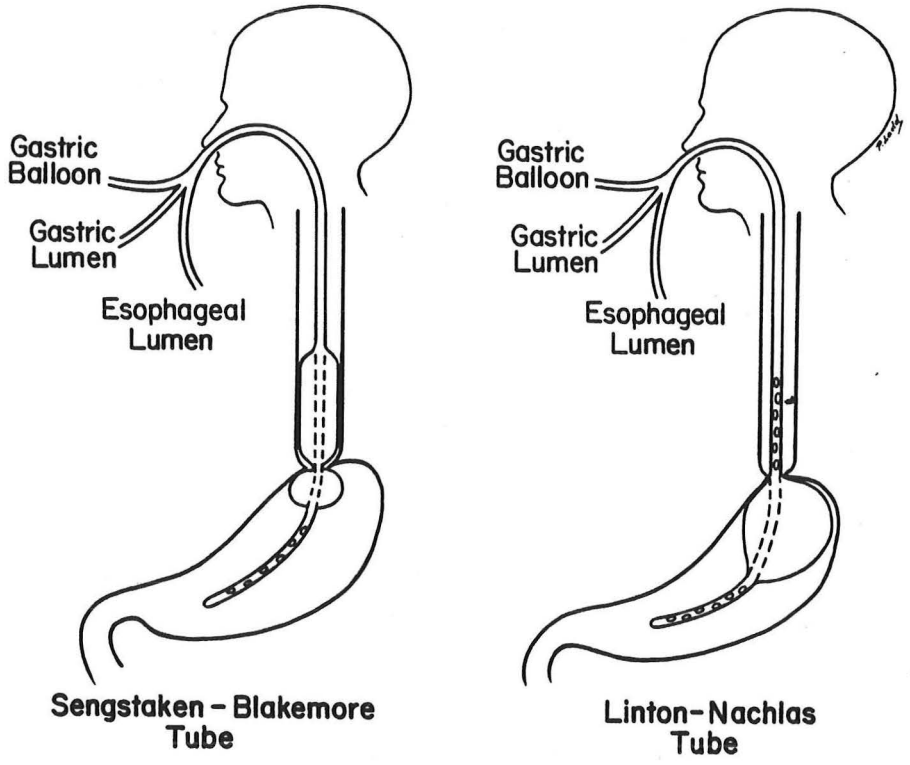
Most patients with varices have cirrhosis, usually alcoholic in origin, although splenic vein thrombosis or hypersplenic states may also result in venous hypertension. When these patients present with bleeding and continue despite lavage and empiric intravenous vasopressin, it is important to perform endoscopy; some patients with varices are bleeding from other lesions [118-120] and it would be inappropriate to continue using therapy designed for varices.

Vasopressin is a potent vasoconstrictor which, by reducing splanchnic blood flow, reduces portal venous pressure. Used originally in doses of 20 units per 10 minutes by intravenous bolus, it effectively stopped variceal bleeding (albeit often only temporarily), [121] but at a cost of some systemic side effects such as hyponatremia, hypertension, cardiac arrhythmias, and decreased cardiac output. It was hoped that by constantly infusing a lower dose directly into the superior mesenteric artery, [122] the desired effect on portal pressure would occur without side effects. Although controlled trials demonstrated the desired effectiveness, some systemic complications remained. [123,124] In addition, local vascular complications related to arteriography were added. Fortunately, it was recognized that a similar low-dose infusion of vasopressin given intravenously also reduced portal pressure. [125] Controlled trials have since demonstrated that an intravenous infusion controls variceal bleeding as well as an arterial infusion but without vascular complications. [126,127] About 60 percent of patients will cease bleeding, although many will rebleed.

If intravenous infusion of vasopressin does not stop the bleeding, what should be tried next? Although there is a suggestion that intra-arterial vasopressin may work when an intravenous infusion does not, [127] the evidence does not justify the delay required to obtain the services of an expert angiographer. Traditionally, the next approach is to use balloon tamponade.

Balloon tamponade of esophageal varices is performed using one of two basic systems (Figure 5). The Sengstaken-Blakemore (S-B) tube is a double-balloon

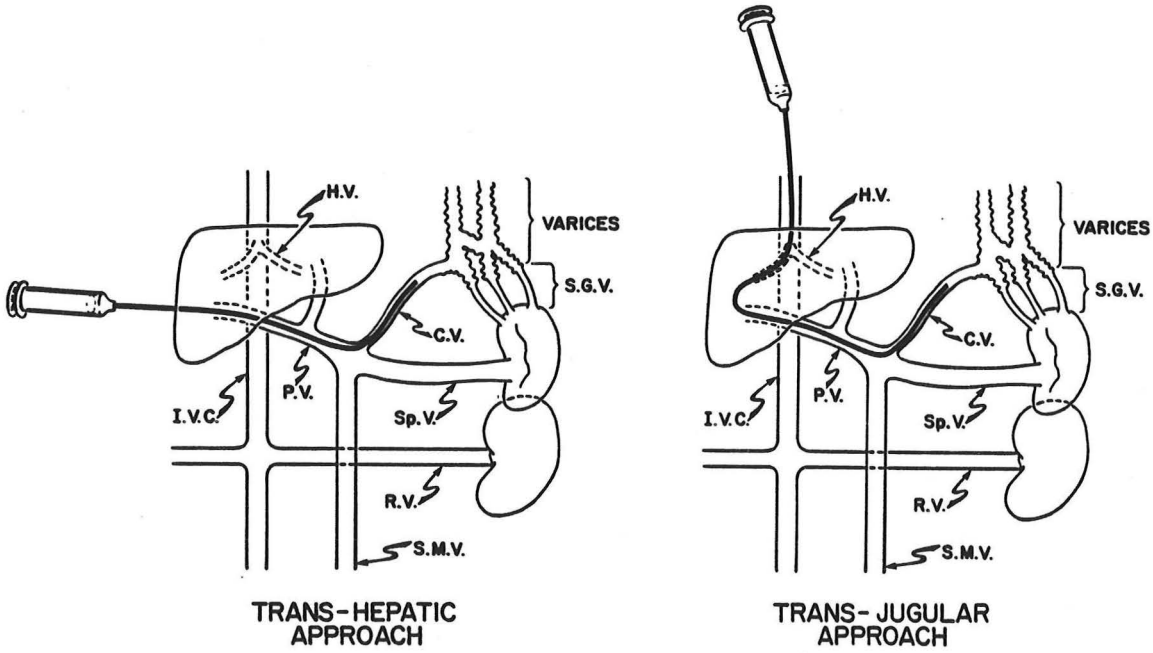
Figure 5. Sengstaken-Blakemore and Linton-Nachlas tubes.



system with an extra tube for gastric suction. One balloon is for inflation in the stomach while the other is for the esophagus. The Linton-Nachlas (L-N) tube uses a single large, gastric balloon but has aspiration tubes both above and below the balloon. The world-wide experience with these tubes has been reviewed recently. [128] Bleeding ceases in 75 to 90 percent of patients if balloon tamponade is used as primary therapy, although it is of interest that the most recent individual series reported a success rate of only 40 percent. [128] This may reflect the fact that, today, the S-B tube is used only after patients have already failed to stop bleeding with intravenous vasopressin. Major complications (esophageal perforation, pulmonary aspiration) occur in almost 15 percent of patients, resulting in death in three percent. The problem of pulmonary aspiration with S-B tubes has been addressed by employing a separate nasogastric tube situated above the esophageal balloon (the Boyce modification) or by using a four-lumen system, in which the extra aspiration tube is built-in. [129] The L-N tube offers no advantage over the S-B tube except possibly in patients with gastric varices. [130]

It must be emphasized that rebleeding after vasopressin or balloon tamponade is frequent and neither technique improves long-term survival. The following three modalities have been proposed not only to stop continuing bleeding when vasopressin and/or balloon tamponade fail, but to improve long-term survival by preventing recurrent bleeding. *Transhepatic obliteration of varices* is accomplished by cannulating the portal vein either percutaneously or by a trans-jugular approach (Figure 6). [131-133] Once the catheter is in the coronary vein

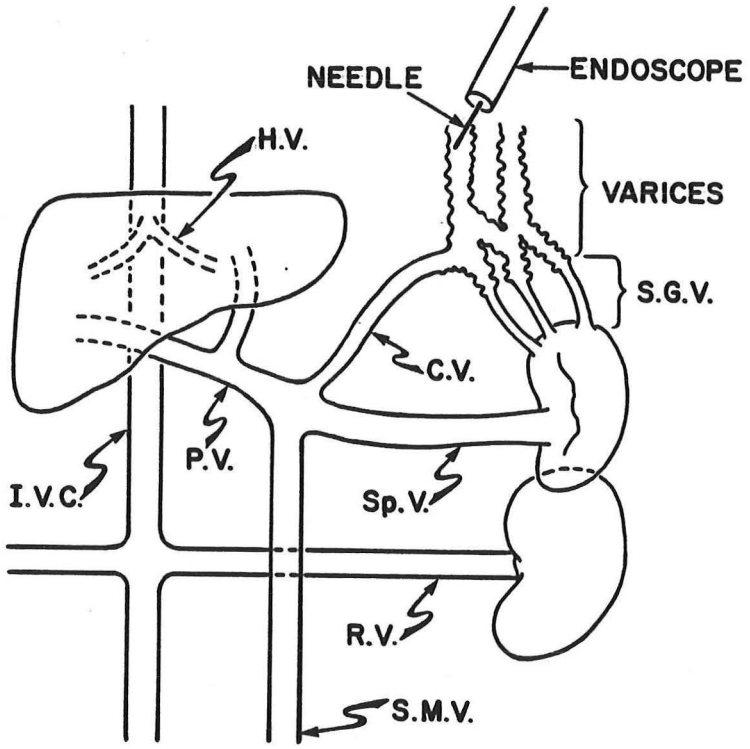
Figure 6. Transhepatic obliteration of varices.



(which feeds esophageal varices) a sclerosing agent or some substance such as gelfoam is injected. The procedure will successfully obliterate the varices and stop active bleeding in 80 to 85 percent of patients. Unfortunately, recanalization or collateral formation is frequent and rebleeding occurs in 70 percent. Complications occur in 20 percent and include intraperitoneal bleeding, pleural effusions and portal vein thrombosis. Because endoscopic sclerosis of varices (see below) accomplishes the same goals in actively bleeding patients without the requirement of a special radiologist and because long term effects are unsatisfactory, the transhepatic approach has little to offer.

Endoscopic injection sclerotherapy was originally described in 1939 [134] but, with the advent of balloon tamonade, vasopressin, and portal-caval shunts, fell out of favor. Since is has become clear that balloon tamponade and/or vasopressin do not control all episodes of variceal bleeding, that recurrent bleeding after these procedures is frequent, and that portal-caval shunts do not improve survival, sclerotherapy is being used once again. Skilled endoscopists (now using flexible endoscopes) can inject and stop actively-bleeding varices 90 percent of the time (Figure 7). [135] Unless a Sengstaken-Blakemore

Figure 7. Endoscopic sclerosis of esophageal varices.



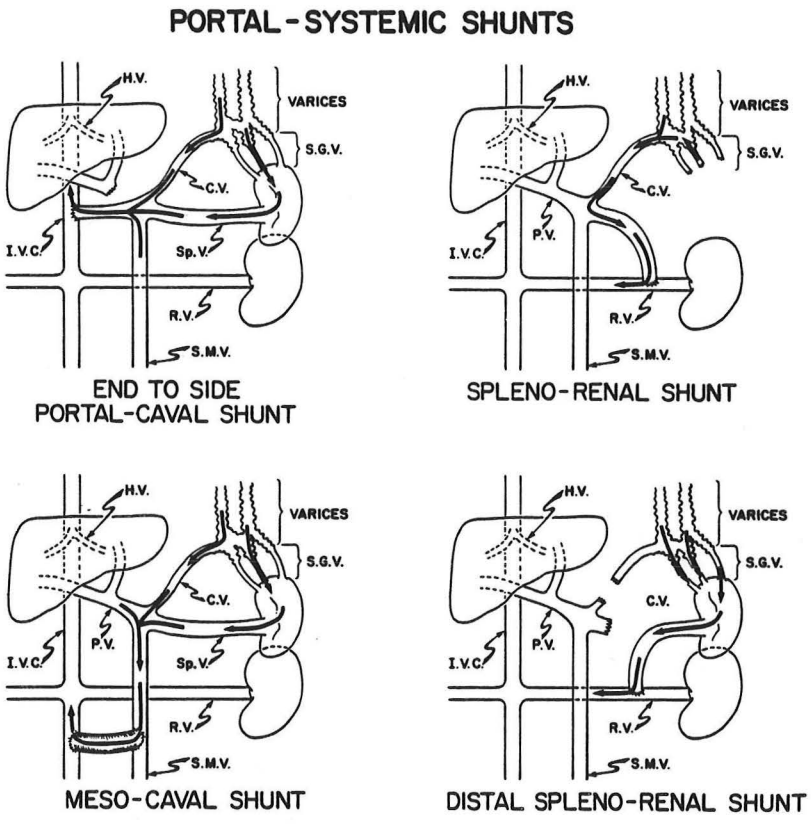
tube is needed for immediate control of exsanguinating hemorrhage, endoscopic sclerosis may well become the next step after vasopressin to control variceal bleeding. Early controlled trials of repeated sclerotherapy in long-term management of patients with varices demonstrate a reduction in the incidence of recurrent bleeding but no improvement in survival. [136,137] The procedure has side-effects, including esophageal ulceration, perforation or stricture. Gastric varices develop in some patients, creating another site for bleeding. Overall complication rate in one study was seven percent of all injections, with 4 of 36 patients ulimately developing an esophageal stricture. [137] More data are needed before the usefulness of this procedure for long-term management can be determined.

Portal-systemic shunts are designed to divert blood in esophageal veins from the high-pressure portal circulation to the low-pressure systemic circulation (Figure 8). When performed emergently to control ongoing bleeding, operative mortality is 50 percent. [138-140] Thus, most surgeons perform emergency shunts only when all else has failed. One notable exception is Orloff who operates on all patients with bleeding varices and reports remarkable long-term survival. [140]

Experience with elective portal-caval, mesocaval, and spleno-renal shunts (shunts which totally divert portal flow) has shown that the incidence of bleeding after a shunt is lower than if a shunt is not done. However, long term survival is not improved whether the procedure is done prophylactically [141-143] or after at least one bleeding episode (the "therapeutic" shunt). [144-147] Rather than die with bleeding, shunted patients die with liver failure and encephalopathy, especially if they are poor-risk patients to begin with. [148] There is evidence that those patients whose hepatic arterial circulation does not compensate for the loss of hepatic portal flow after shunting do less well than those who maintain hepatic blood flow after shunting. [149] Because total hepatic flow may be important, the current shunting procedure is one that decompresses only veins of the esophagus and stomach, the "selective" distal spleno-renal shunt of Warren and Zeppa. Controlled trials comparing this shunt with no shunt have not been reported. Those studies that compare selective to total shunts disclose no difference in recurrent variceal bleeding or long-term mortality. [150-152] The only benefit of the selective shunt appears to be a lower incidence of hepatic encephalopathy; the disadvantage is that it requires great surgical expertise.

In summary, no technique has been proven to alter the long-term course of most patients who have bled from esophageal varices. It is continuing liver failure which ultimately claims these patients, especially those with alcoholic

Figure 8. Portal-systemic shunts.



cirrhosis who continue to drink. Recurrent bleeding or hepatic encephalopathy are issues more relative to quality of life, days spent in the hospital, or the drain on blood banks than to long-term survival. Although there may be patients in whom prevention of recurrent bleeding or encephalopathy will prolong life (for example, nonalcoholics with preserved liver function), they have not been well defined.

Mallory-Weiss Tears - Arterial bleeding from an acute laceration of gastroesophageal mucosa [153] accounts for 10 to 15 percent of upper GI bleeding episodes. [154-158] Retching is often, but not always, implicated in Mallory-Weiss tears and excessive intake of alcohol (with or without concomitant aspirin ingestion) is noted in almost 70 percent of patients with this lesion. Most patients cease bleeding spontaneously and rebleeding is unusual. For continuing bleeding *selective infusion of vasopressin* into the left gastric artery will succeed in many instances. [80-82] (Intravenous vasopressin is ineffective in arterial bleeding. [65,82,159]) Rarely, direct oversew of the bleeding lesion at surgery is necessary, although some believe that transcatheter embolization of the bleeding lesion with Gelfoam should be attempted first. [160]

Acute Gastritis - Hemorrhagic gastritis is a relatively uncommon cause of acute upper GI bleeding prompting admission to the hospital. Recent series suggest it is the cause for about 5 percent of such admissions. [22,154,155] Alcohol and aspirin are frequently implicated although aspirin alone usually causes only mild erosions and occult bleeding (see page 30). Hemorrhagic gastritis as a result of severe underlying illness (ie., "stress gastritis" in the face of sepsis, shock, burns, post-operative states, respiratory failure, etc.) is a problem primarily of patients already hospitalized for other reasons. [154,161]

If a patient continues to bleed from gastritis, surgery should be avoided if at all possible, since operative mortality is very high. [162] Although antacids in enough volume to maintain gastric pH at 7.0 have been reported to stop bleeding from acute gastritis, the studies are uncontrolled. [42,43] *Selective infusion of vasopressin* via the left gastric artery will produce cessation of bleeding in 75 percent of patients. [81,82,123,163] It is re-emphasized that vasopressin, even selectively infused, is not without side-effects. Systemic side-effects, as well as gastric infarction, [164] have been described.*

Fortunately, few patients today require therapy for severe bleeding from stress gastritis. [162] Controlled trials of antacid or cimetidine regimens in patients under varying forms of stress suggest that bleeding will not occur if gastric pH is kept above 4.0 to 5.0. [165-172] This is more easily accomplished with increasing doses of hourly antacid than with increasing doses of cimetidine. [173,174] While 95% of patients can be "controlled" to pH 4.0 or higher with a potent antacid in doses of 60 ml per hour, [173] cimetidine up to 300 mg every three hours leaves over 25 percent of patients uncontrolled and supplemental antacids must be given. [173,174] This is especially true in patients with sepsis. Two widely quoted trials in prevention of stress bleeding have been performed by the group from Harvard. [168,170] Results of their studies are shown in Table 4. It is of interest that although antacids can more effectively maintain gastric pH over 4.0, and thus more often prevent bleeding, overall mortality is unchanged. These patients are so ill that whether they bleed or not makes little difference in their overall prognosis.

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* Another non-operative form of therapy may be the use of prostaglandin analogs. (Personal communication from Jon Isenberg, M.D.)

Table 4. Effect of antacid and cimetidine in preventing stress bleeding.

	Regimen		
	Control	Antacid	Cimetidine
Dose	-	Up to 120 ml per hour to keep pH > 3.5	Up to 400 mg q4 hrs. to keep pH > 3.5
Proportion bleeding:			
Ref. 168	12/49	2/51	-
Ref. 170	-	0/37	7/38

A relatively inexpensive approach to prophylaxis is hourly administration of a potent magnesium and aluminum hydroxide antacid via nasogastric tube to patients at risk for stress bleeding. To ease the strain on nursing personnel this can be given as a constant drip at a rate of 30 to 60 ml per hour. If the pH cannot be maintained at 4.0 to 5.0, cimetidine can be added in doses up to 300 mg every 3 hours. A constant infusion of cimetidine at 50 to 100 mg per hour will result in smoother control of pH by maintaining a more constant blood level. [173] If diarrhea is the only problem, the antacid can be alternated with one composed primarily of aluminum hydroxide.

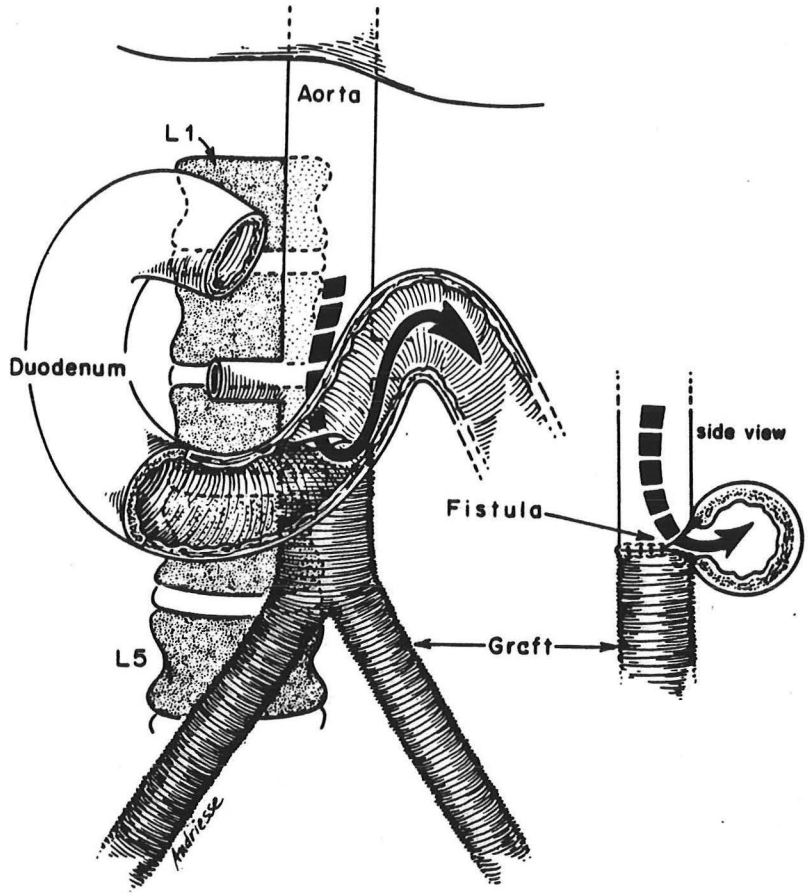
Hematobilia - Causes of arterio-biliary fistulas include trauma, liver biopsy, cancer, hepatic artery aneurysm, hepatic abscess and gallstones. The classic presentation is with upper GI bleeding accompanied by biliary colic and jaundice. The diagnosis is made endoscopically by seeing blood coming from the Ampulla of Vater and/or by diagnosic hepatic arteriography. Therapy is with *selective arterial embolization* [175] and, if that fails, by *hepatic artery ligation.*

Neoplasms - Upper GI neoplasms are responsible for only one to two percent of acute upper GI bleeding episodes. [22,154,155] Occasionally such lesions will continue to bleed and in some instances will prompt surgical intervention. Alternative therapy for patients with bleeding tumors includes *selective arterial embolization* [176] (vasopressin will not work) or perhaps *electro - or laser photocoagulation.*

Arterial-enteric fistulas - Aneurysms of the aorta and branches of the celiac artery may occasionally form a fistulous connection to the upper GI tract. [177,178] Aortic aneurysms usually involve the duodenum while aneurysms of the celiac branches involve the stomach, duodenum and liver. Aorto-enteric fistulas almost always produce a premonitory episode or "herald bleed" hours to occasionally weeks before catastrophic hemorrhage [177] and smaller-vessel-enteric fistulas may cause recurrent bleeding for years. [178] Diagnosis of an aneurysm can be made only with an index of suspicion and careful arteriography. Surgical resection is the therapy.

A more common circumstance is a fistula between a prosthetic aortic graft and the intestine (again, primarily duodenum) (Figure 9). These most commonly involve the proximal anastomosis of the graft and often have associated false aneurysms; localized infection may also play a possible role. As with primary aorto-duodenal fistulas, a "herald bleed" is common and may include back

Figure 9. Fistula between prosthetic aortic graft and duodenum (From Ref. 181).



pain. [179-182] Any patient with a prosthetic graft in place who presents with upper GI bleeding must be assumed to have a fistula until proven otherwise. Endoscopy is performed as soon as possible. Occasionally the fistula will be seen [183] but usually it is not. More importantly, other bleeding lesions are sought; if none are found, it must be assumed a fistula is present and surgery performed. Arteriography will only occasionally diagnose aortoenteric fistulas (ie, visualization of a false aneurysm or active bleeding). Therefore, arteriography has no role in patients in whom endoscopy finds no other lesions. A positive arteriogram will only confirm the clinical decision to operate while a negative exam is too unreliable to change the decision. It may be worth the effort to perform arteriography (even with the low yield) in patients in whom endoscopy detects another lesion and a tentative decision has been made <u>not</u> to operate. Here, a positive arteriogram would change the decision.

<u>Vascular anomalies</u> - These are unusual causes of acute upper GI bleeding and, when present, almost always result in recurrent bleeding. They are discussed in a special section on page 31.

ACUTE LOWER GI BLEEDING

Lower GI bleeding, defined as bleeding from a source below the ligament of Treitz, differs from upper GI bleeding in three basic ways. First, patients are older. Second, the presenting manifestation is hematochezia; only occasionally will melena occur. Third, unlike upper GI bleeding, new diagnostic techniques (arteriography and colonoscopy) have prompted important changes in therapeutic approach. In patients with acute, massive bleeding there appears to have been a reduction in mortality.

From the mid 1950's through the late 1960's, patients with acute massive or recurrent lower GI bleeding often underwent segmental left colectomy. This was based on the belief that diverticulosis accounted for most of the bleeding episodes and on the fact that most diverticula are in the left colon. This approach resulted in a 50 percent incidence of recurrent bleeding and, in patients with massive bleeding, a mortality of about 20 percent. [184,185] Obviously, many patients were bleeding from the right colon or above. Therefore, surgeons turned to subtotal colectomy with ileo-proctostomy. The incidence of recurrent bleeding fell, mortality dropped to 10 percent, [184,185] but many patients had post-operative diarrhea. Today, precise information obtained from angiography and colonoscopy allows the surgeon once again to perform segmental resections, but now many of them involve the right colon and often the lesion is not a diverticulum. Post-operative rebleeding is negligible, mortality with massive bleeding is five percent or lower, and post-operative diarrhea is not a problem. [186]

Better management of patients with lower GI bleeding has come about because of the following:

1. Selective mesenteric arteriography in patients with massive, continuing hemorrhage localizes the precise area of the bowel which is bleeding. In the case of diverticula, this is from the <u>right</u> colon 70 percent of the time, [186-194] one reason segmental left hemicolectomy was often unsuccessful. In other instances the bleeding is from a colonic lesion other than a diverticulum or from a noncolonic lesion, such as a duodenal ulcer or small bowel tumor. [193] In addition, arteriography allows control of many bleeding lesions with vasopressin.
2. A previously unrecognized entity, cecal angiodysplasia, has been increasingly detected by arteriography. These subtle vascular anomalies undoubtedly accounted for many cases of acute or chronic bleeding attributed to diverticulosis and are another reason blind left hemicolectomy was associated with such a high incidence of failure. These lesions may sometimes be seen by colonoscopy and are probably what some surgeons have called "cecal erosions". [195]
3. Colonoscopy in patients with lower GI bleeding whose barium enema is "negative" or shows only diverticulosis detects a substantial number of lesions, including carcinoma. [196-199] Before colonoscopy, such patients may have been sent home with "no diagnosis" or "bleeding diverticula". Some would have undergone blind left hemicolectomy.

<u>Diagnostic Approach to Acute Lower GI Bleeding</u>

<u>History and Physical Examination</u> - Important historical information includes a prior history of hemorrhoids or inflammatory bowel disease. Have there been prior episodes of bleeding (angiodysplasia)? Has there been pain or diarrhea (colitis)? Has there been weight loss or a change in bowel habits (colon cancer)? Physical examination should include a search for skin lesions of inflammatory bowel disease or an abdominal mass (cancer)? Is there a mass on rectal examination?

Anoscopy and Sigmoidoscopy - Every patient with presumed lower GI bleeding should undergo anoscopy and sigmoidoscopy to look for bleeding hemorrhoids, anal fissure, rectal ulcer, colitis, or a rectal cancer. The procedure is difficult when bleeding is brisk and it is often impossible to tell whether blood is coming from above the sigmoidoscope or is refluxing from a lesion below (ie., hemorrhoids).

Nasogastric Aspirate - If a definite diagnosis is not made by sigmoidoscopy, an upper GI lesion should be excluded by nasogastric aspiration. Remember that an actively bleeding duodenal ulcer or aorto-duodenal fistula may produce hematochezia without a positive nasogastric aspirate. Even when bowel sounds do not seem hyperactive and the BUN is not elevated, any suspicion of an upper GI source should prompt endoscopy, especially if arteriography is imminent.

Barium Enema - Contrast studies of the colon have no place in the management of acute, on-going lower GI bleeding. Not only may the bleeding lesion be missed but results may be misleading if only diverticula are seen. Furthermore, a colon full of barium makes subsequent arteriography difficult. Some have proposed the barium enema as a therapeutic tool, to tamponade the bleeding vessel; [200] most radiologists do not agree with this practice. If bleeding ceases, which is the usual case, [186] a double-contrast barium enema is a helpful procedure. Although other procedures (such as colonoscopy) will usually be done regardless of the results, a barium enema may assist the colonoscopist by demonstrating suspicious areas and will sometimes disclose lesions missed by colonoscopy or arteriography.

Arteriography - There are two situations in which diagnostic arteriography is helpful. First, in the patient with massive on-going hemorrhage, arteriography can detect the site of bleeding (ie, right or left colon, small bowel, upper GI tract) and in many instances determine whether the lesion is a diverticulum, vascular anomaly, cancer, or an ulcer. Beyond directing the surgeon to the correct location for the correct operation, selective arteriography permits the infusion of vasopressin directly into the bleeding artery. The causes of lower GI bleeding brisk enough for extravasation to be noted during arteriography are shown in Table 5. [186,187,190-194] Diverticulosis is the most common,

Table 5. Causes of "lower" GI bleeding when extravasation is noted at angiography. (From references 189, 190, 193-197).

Diverticulosis	70%
Angiodysplasia	10%
Peptic Ulcer	5%
Meckel's Diverticulum	3%
Neoplasms	3%
Vascular-enteric Fistula	2%
Jejunal Diverticulum	2%
Other	5%

but the five percent incidence of peptic ulcer emphasizes the need to perform endoscopy before arteriography.

Second, arteriography may define lesions with abnormal vasculature even if extravasation is not noted. This is useful in patients with acute massive bleeding that has slowed by the time of arteriography or in patients with several recurrent bouts of acute bleeding. Lesions likely to be found in this situation include ileo-colic angiodysplasia, colon cancer, small bowel arterio-venous malformations, and small bowel leiomyomas or leiomyosarcomas. [192,193]

Colonoscopy - Colonoscopy is of value in two situations. First, in some patients acute massive bleeding will slow enough to allow emergent colonoscopy. [186,201] The same spectrum of lesions will be found in this way as are found with arteriography. Second, colonoscopy will detect a substantial number of lesions in patients with acute lower GI bleeding which has ceased and in whom a barium enema is negative or shows only diverticulosis. [196-199] The most frequent lesions found in four series are shown in Table 6, although

Table 6. Lesions found by colonoscopy in patients with lower GI bleeding in whom barium enema was negative or showed only diverticulosis.

Reference	Number Studied	Cancer	Polyps	Colitis	Angiodysplasia
199	199	21	32	24	4
200	196	24	29	16	2
201	212	26	35	19	15
202	247	19	37	11	10
	854	90 (11%)	133 (16%)	70 (8%)	31 (4%)

double-contrast barium enemas were not performed in all patients. Furthermore, since these patients were not actively bleeding, there is no guarantee the lesions found, especially polyps, were the cause of bleeding. The frequency of cancer found in these studies underscores the importance of seeking a diagnosis in patients with rectal bleeding.

Radioisotopic Scanning - The use of radioisotopes in active bleeding has been discussed on page 12. There is one special situation pertinent to lower GI bleeding - Meckel's diverticulum. [202,203] In this situation, Tc-99 pertechnetate may not only extravasate from an actively bleeding Meckel's diverticulum but may also be taken up by ectopic gastric mucosa in one that has ceased bleeding. This procedure is known to produce false positive and false negative results.

Suggested Overall Diagnostic Approach - Sigmoidoscopy and nasogastric aspiration are performed. If a patient continues to bleed, and has required three or more units of blood transfusions, (25 percent of cases), [186,204] the following sequence is recommended:

1. Perform upper GI endoscopy to exclude an upper GI lesion.
2. If bleeding slows sufficiently, perform colonoscopy after a fluid purge.

3. If bleeding remains brisk, perform mesenteric arteriography beginning with the superior mesenteric artery (since most lesions will be found in the right colon) and progressing if necessary to the inferior mesenteric and celiac arteries (Table 5).
4. If extravasation of contrast is seen, infuse vasopressin. If bleeding continues despite vasopressin, surgery should be performed before blood loss has become too great. If bleeding ceases, a decision regarding elective surgery can be made after further evaluation.
5. If no extravasation is noted, but bleeding continues, an exploratory laparotomy and a subtotal colectomy will most likely be needed.

If bleeding ceases spontaneously, (which happens 75 percent of the time [186,204]), a different approach is warranted:
1. Withold diagnostic procedures for 48 hours.
2. If rebleeding occurs during this time perform upper GI endoscopy followed by arteriography or colonoscopy.
3. If no rebleeding occurs, perform an air contrast barium enema followed by colonoscopy (Table 6). If barium enema and colonoscopy are negative, an upper GI source must be excluded. Consider arteriography (to look for lesions with abnormal vasculature) if there have been prior episodes of lower GI bleeding and if the patient is an operative candidate. Arteriography should not be a routine procedure for first-time bleeding.

Approach to Specific Lower GI Bleeding Lesions

Diverticulosis - Bleeding occurs in only three to five percent of patients with diverticulosis [184] but, because this entity is so common in western society, it is the most important cause of lower GI bleeding. Diverticulosis accounts for 70 percent of the cases of lower GI bleeding in which arteriography detects extravasation (Table 5) and perhaps 40 to 50 percent of all cases. [193] Many of these, however, are diagnoses of exclusion (ie., only diverticulosis is seen by barium enema and no other bleeding site is found by arteriography or colonoscopy). Bleeding is abrupt in onset, painless, often massive and often from the right colon. Twenty percent of patients will continue bleeding, 20 percent will stop and then rebleed in hospital, and the remaining 60 percent will cease and often never have another bleeding episode. [193] For those with active bleeding, selective mesenteric arteriography locates the site (70 percent right colon) and, if vasopressin is infused, the bleeding ceases at least temporarily in 90 percent of patients. [188,194] Many of these patients will not require further therapy (Table 7). Surgery (segmental resection) is reserved for

Table 7. Long-term outcome of patients with diverticular bleeding which ceases during vasopressin infusion (Ref. 188).

Discharged After Partial Colectomy For:	No.	Further Bleeding	No Further Bleeding
- Rebleed in Hospital	5	0	5
- Prior bleeding	5	0	5
No Surgery	12	3	9

Figure 10. Anatomic relationship between dome of diverticulum and colonic artery (From Ref. 205).

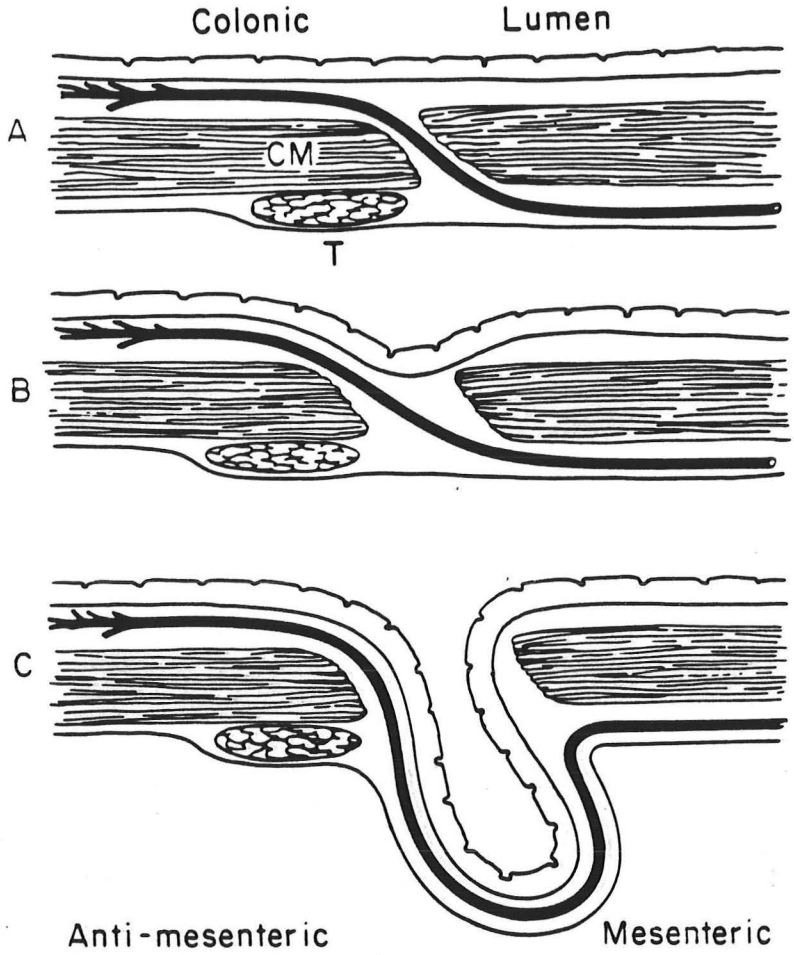
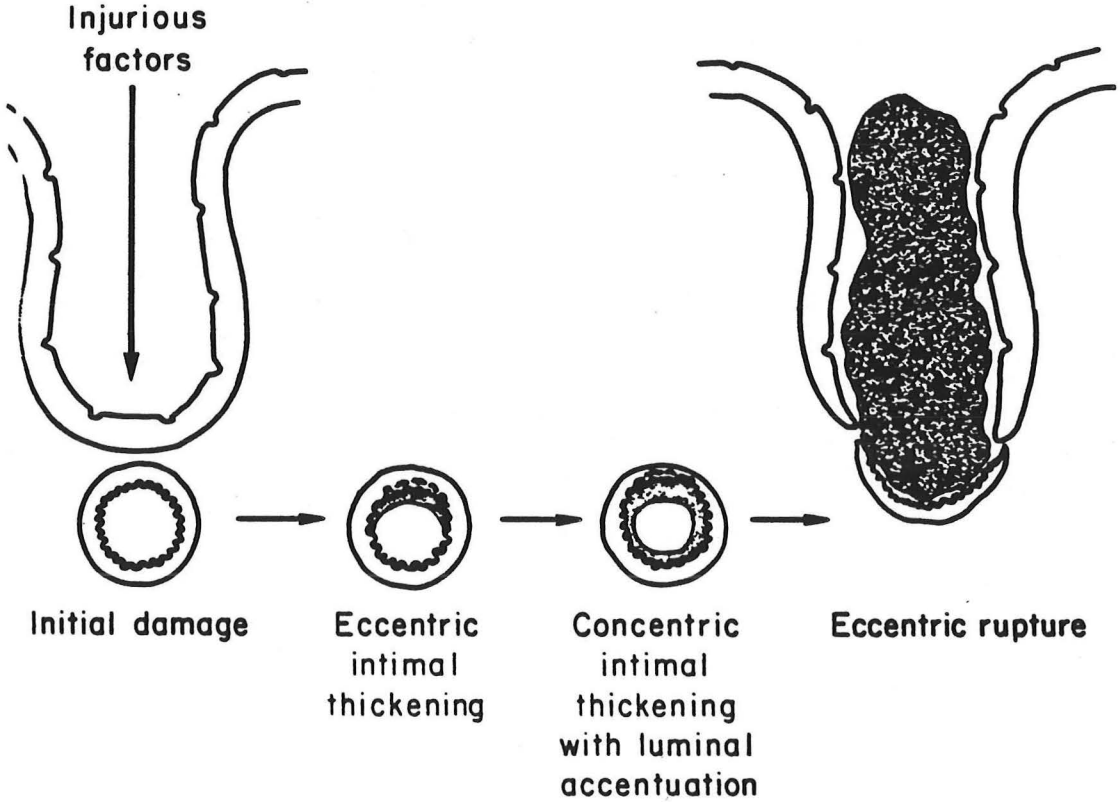


Figure 11. Mechanism of arterial weakening and rupture (From Ref. 205).



those patients who fail a trial of vasopressin, who rebleed in hospital, or who have had prior episodes of proven diverticular bleeding. Caution must be used in operating on such patients without angiographic or colonoscopic documentation of the bleeding site.

Bleeding from diverticula is believed to occur after years of pressure on a penetrating colonic artery by the dome of the diverticular pouch (Figures 10 and 11). [205] With time, there is eccentric breakthrough of the vessel which ruptures into the diverticular sac. Since the artery is large, bleeding tends to be copious. Since the artery is single, bleeding usually does not recur if a thrombus forms and becomes firmly affixed to the vessel wall. [208]

Vascular Anomalies - Vascular anomalies (especially angiodysplasia) are an important cause of lower GI bleeding. They are responsible for 10 percent of massive, continuing bleeding (Table 5) but most often produce chronic or recurrent bleeding (see page 31).

Neoplasms - Neoplasms do not often produce exsanguinating hemorrhage, but rather tend to present with chronic, occult bleeding or with intermittent bouts of acute, self-limited bleeding. Small bowel tumors are rare and relatively inaccessible; arteriography is needed in many cases (see page 30). Colon cancer is common and is readily diagnosed by barium enema and/or colonoscopy.

Other Lesions - Hemorrhoids are probably the most common cause of lower GI bleeding, but usually only in the form of intermittent episodes producing small amounts of bright red blood on the outside of formed stool or on toilet tissue. Only occasionally will massive bleeding occur. Treatment for hemorrhoids is with sitz baths, lubricating suppositories (with or without corticosteroid), and stool softeners. If problems continue, "banding" or hemorrhoidectomy may be necessary. Management of bleeding from ischemic bowel disease or inflammatory bowel disease is generally directed toward the basic disease process. Solitary ulcers of the rectum and cecum, the latter especially in patients with renal failure, [206,207] are infrequent causes of lower GI bleeding. Arterial-enteric fistulas occur in the small bowel and colon; [208] as with upper GI lesions, diagnosis is by arteriography. Intussusception is almost always accompanied by abdominal pain during which a plain film of the abdomen or small bowel barium x-ray will be diagnostic.

OCCULT GI BLEEDING

For purposes of this discussion, occult bleeding refers to bleeding manifested only by a guaiac positive stool. Because it is not obvious to the patient, such bleeding is usually chronic. One important cause of chronic, occult bleeding is gastro-duodenal damage by various drugs (see below). However, one must be cautious in ascribing bleeding to drugs since neoplasms (especially colonic) also present with chronic occult bleeding; [209] detection of cancer at this stage in otherwise asymptomatic patients often yields excellent long-term prognosis. On the other hand, a full work-up for occult bleeding is expensive and uncomfortable. One must therefore use common sense in deciding whom to evaluate. Factors favoring such an evaluation include no history of drug ingestion, age over 40 years, and the presence of any symptoms. If a decision is made not to proceed with diagnostic studies, the patient must be followed carefully.

Unless a patient has upper GI symptoms, evaluation should begin with sigmoidoscopy, barium enema, and colonoscopy looking for a colonic neoplasm or inflammatory bowel disease. If evaluation of the colon is negative, an upper GI x-ray should be performed looking for peptic ulcer or a neoplasm. Endoscopy is often performed but might be delayed in a patient who is taking drugs known to produce bleeding.

Drug Induced GI Bleeding

There is a well-accepted relation between aspirin ingestion (especially with concommitant alcohol) and GI bleeding. [210,211] Only some bleeding episodes are major and only some are related to chronic peptic ulcer. [211] For the most part aspirin produces mild, occult bleeding [212,213] as a result of acute gastroduodenal mucosal lesions. [214] These lesions are seen endoscopically within one hour of oral administration and (with repeated doses) maximal damage occurs by 24 hours. [215] The effect of aspirin is local, since enteric-coated aspirin (which produces equivalent blood salicylate levels) is much less injurious. [214,216] Likewise, intravenous aspirin does not produce the histologic effects seen with oral aspirin. [217] The mechanism by which aspirin produces mucosal lesions is complex. Acid plays a role since neutralization of gastric contents will prevent mucosal injury.* [218] The role of acid is most likely only permissive, however, since doses of cimetidine or anticholinergics which do not reduce acid secretion also prevent mucosal injury in animals. [219,220] More important may be aspirin's well-known ability to inhibit biosynthesis of endogenous prostaglandins. [221,222] This theory is supported by three lines of evidence. First, mucosal lesions are produced by non-steroidal anti-inflammatory agents which also inhibit prostaglandin biosynthesis. [223] Second, acetaminophen, which has less effect on prostaglandin synthesis [222] is much less injurious to gastric mucosa and is not associated with GI bleeding. [222 224] Third, oral administration of prostaglandin E_2 (which has no anti-secretory properties) prevents mucosal bleeding induced by aspirin or indomethacin. [225-227]

Most patients on regular aspirin or non-steroidal anti-inflammatory agents (NSAIA) will have no problems. If bleeding occurs with regular aspirin, an enteric-coated preparation may be used. If bleeding occurs with a NSAIA, antacid, cimetidine or (in the future) prostaglandin may be administered. Finally, new NSAIA are being developed which may be less injurious to gastroduodenal mucosa. [228]

GI BLEEDING OF "OBSCURE" ORIGIN

A few patients with chronic, occult or recurrent, acute GI bleeding remain without a diagnosis despite repeated upper GI x-rays, barium enemas, endoscopy and colonoscopy. Some patients may be bleeding from the small bowel, a region poorly evaluated by standard diagnostic procedures. Many are bleeding from vascular anomalies which may involve all areas of the GI tract. These lesions are either not grossly visible or are subtle and often overlooked at endoscopy/colonoscopy. Techniques available to detect obscure causes of GI bleeding include radionuclide scanning, small bowel infusion x-rays, and arteriography. Asymptomatic patients with bleeding that requires no blood transfusion and who respond to oral iron need only undergo a small bowel infusion x-ray. [229]

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* It should be noted that most commercially-available "buffered" aspirin compounds do not effectively neutralize gastric contents and produce mucosal lesions similar to regular aspirin. [214,216]

This technique will not detect vascular anomalies but will often detect small bowel neoplasms and Meckel's diverticula. Radionuclide scanning may also detect Meckel's diverticula in younger patients.

If there are symptoms or if bleeding is severe enough to require transfusions, mesenteric arteriography should be performed in addition to a small bowel infusion x-ray. This is best done as soon a possible after bleeding is noted in order to detect luminal extravasation.* However, even if bleeding has ceased, arteriography may disclose vascular anomalies or tumor vessels. [230,231]

Vascular Anomalies

It is now recognized that vascular anomalies (excluding hemangiomas which are neoplasms) are the most frequent cause of obscure GI bleeding. [230,231] There is much confusion over nomenclature of these lesions but for clinical purposes they may be divided into two broad groups, those with and those without associated skin lesions.

Vascular Anomalies With Associated Skin Lesions - These include rare entities such as the hereditary syndromes of Osler-Weber-Rendu (hereditary hemorrhagic telangiectasia) and the Blue Rubber Bleb Nevus and the acquired CRST syndrome. Lesions are found throughout the GI tract and are usually visible endoscopically. Surgical resection is at times performed but, since the lesions are often multiple and diffuse, laser photocoagulation may prove to be more satisfactory therapy. [232]

Vascular Anomalies Without Associated Skin Lesions - The frequency of these lesions was unrecognized until the advent of selective mesenteric arteriography. [66,233,234] It appears that there are two subgroups of vascular anomalies without associated skin lesions. [235] They are similar arteriographically and both are difficult to see with the naked eye . They differ in terms of histology, location in the GI tract, age of patients in whom they are found, and probable etiology. [236-238]

The less common of the two, accounting for less than 20 percent of vascular anomalies, is the arterio-venous malformation. These consist of dilated, thick-walled arteries and nondilated, thick walled ("arterialized") veins which communicate with each other. [237] They may be found throughout the GI tract but are most frequent in the upper intestine. [239,240] Because they are often found in younger patients, their etiology is believed to be congenital. Diagnosis is by arteriography and, at times, endoscopy. Although poor-risk patients may respond to arterial embolization, most are treated with segmental surgical resection. Endoscopic transillumination of the bowel may assist the surgeon in localizing the lesion.

Angiodysplasia [241-243] (or vascular ectasias [237,244,245]) make up the majority of vascular anomalies (80 percent). These lesions are even smaller than those described above and were not appreciated (except in retrospect [195]) until arteriography assumed a major role in the evaluation of patients with lower GI bleeding. They occur almost exclusively in older patients (and are thus believed to be acquired rather than congenital) and have been most often noted in the distal ileum, cecum, and ascending colon. However, now that radiologists and endoscopists are attuned to these lesions, they are being reported to occur in the upper GI tract [246] and sigmoid colon. [247] Proof that some or all of

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* It is important that patients understand the necessity of informing their physician as soon as bleeding begins so that the arteriography team can be assembled before the patient arrives at the hospital.

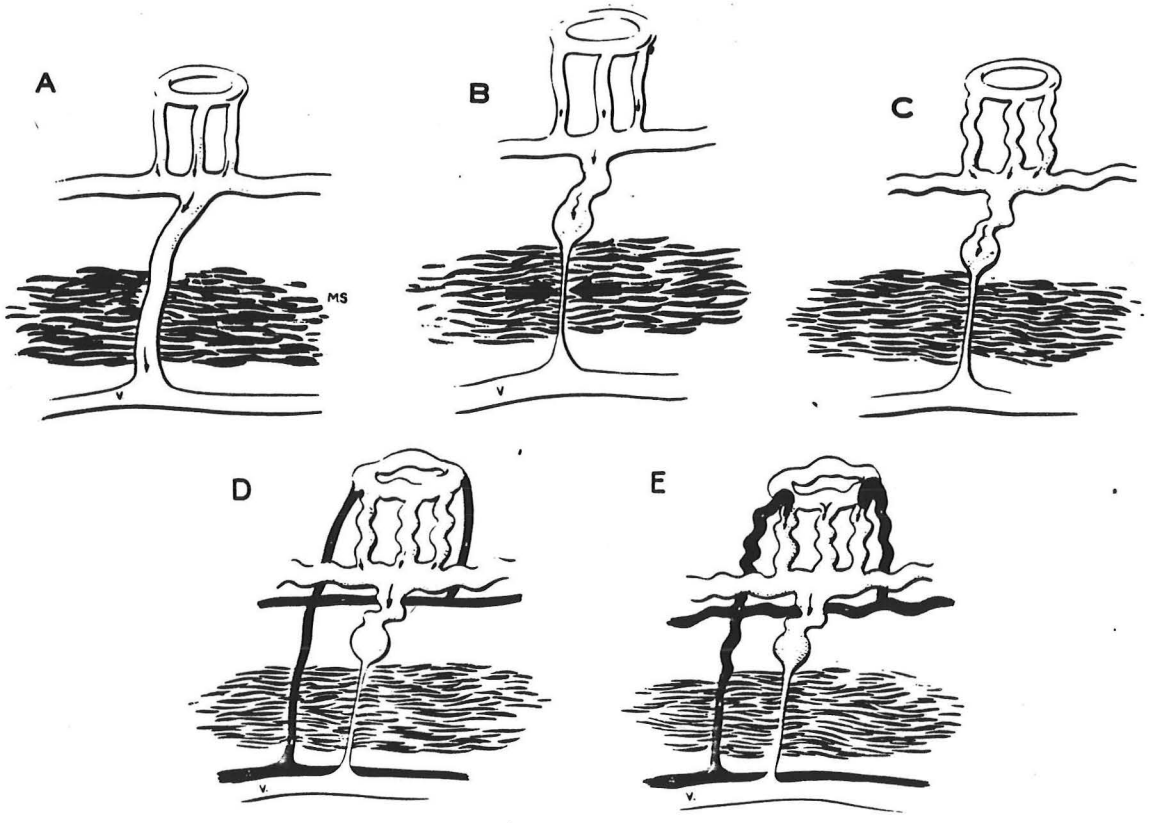
these lesions are not actually arterio-venous malformations awaits histologic evaluation. There appears to be an association among angiodysplasia, aortic stenosis, and unexplained GI bleeding [242,246,248] but the mechanism of this association is not known.

The arteriographic criteria of angiodysplasia include clusters of small arteries, visualization of a vascular tuft, and early and prolonged opacification of a draining vein, usually the ileocolic. [242,243] Very seldom will bleeding be brisk enough or persistent enough for extravasation of contrast material to be noted. When visualized endoscopically angiodysplasias are flat, bright red, and fern-like. [249-251]

Angiodysplasias are seen grossly and histologically only with meticulous examination and careful sectioning, and even then lesions may be overlooked. It has required injection of the blood vessels of resected specimens with silicone rubber to determine histologic characteristics. The most prominent, and earliest, findings are submucosal, where there are ectatic and tortuous veins. [237] Submucosal arteries are usually normal, unlike arterio-venous malformations. In most instances, there are also abnormal mucosal vessels, from just a few ectatic capillary rings surrounding the crypts to large "coral reef-like" lesions. In the most advanced lesions, these ectatic vessels constitute the bulk of the mucosa and are not protected by colonic epithelium from potential rupture.

There is no proven etiology for angiodysplasia, but the hypothesis put forth by Boley is plausible. [244] According to this theory, (Figure 12), there is

Figure 12. Diagrammatic illustration of proposed concept of the development of cecal vascular ectasias. A, normal state of vein perforating vascular layers. B, with muscular contraction or increased intraluminal pressure the vein is partially obstructed. C, after repeated episodes over many years the submucosal vein becomes delated and tortuous. D, later the veins and venules draining into the abnormal submucosal vein similarly involved. E, ultimately the capillary ring becomes dilated,the precapillary sphincter becomes incompetent, and a small arteriovenous communication is present through the ectasia (From Ref. 244).



chronic, low grade obstruction of submucosal colonic veins where they traverse the muscularis propria. This results in, first, ectasia of submucosal vessels; second, dilatation of mucosal venules and capillaries; and last, loss of precapillary sphincters producing small arterio-venous shunts.

Clinically, bleeding from angiodysplasias is self-limited but chronic or recurrent. Those few who bleed massively may demonstrate extravasation of arteriographic contrast material and may respond to vasopressin. In most situations, however, there is no evidence of active bleeding and no proof that an arteriographically documented angiodysplasia is the actual source of bleeding. How should these patients be managed? First, other lesions (such as carcinoma of the colon, small bowel tumors, or upper GI lesions) must be fully excluded. Second, bleeding must be important enough to warrant surgery (ie., chronic anemia, transfusion requirements). If these criteria are met, a right hemi-colectomy will prevent further bleeding episodes in about 80 percent of patients. [236,243,245] If rebleeding occurs, other angiodysplasias must be sought. However, some patients will be bleeding from other sources (such as left-sided diverticula [245]) and may never have bled from an angiodysplasia. Boley found submucosal ectasias in 8 of 15 elderly patients without GI bleeding and in 4 of these 8 there were also mucosal ectasias. Thus, these lesions are probably very common, producing bleeding only in those with more striking mucosal involvement. This observation should prompt restraint in looking for angiodysplasia and removing them if found. It is possible that electro-or laser photo-coagulation will provide an alternative to surgery in the management of angiodysplasia, [251] although these techniques must be considered experimental and reserved for highrisk patients.

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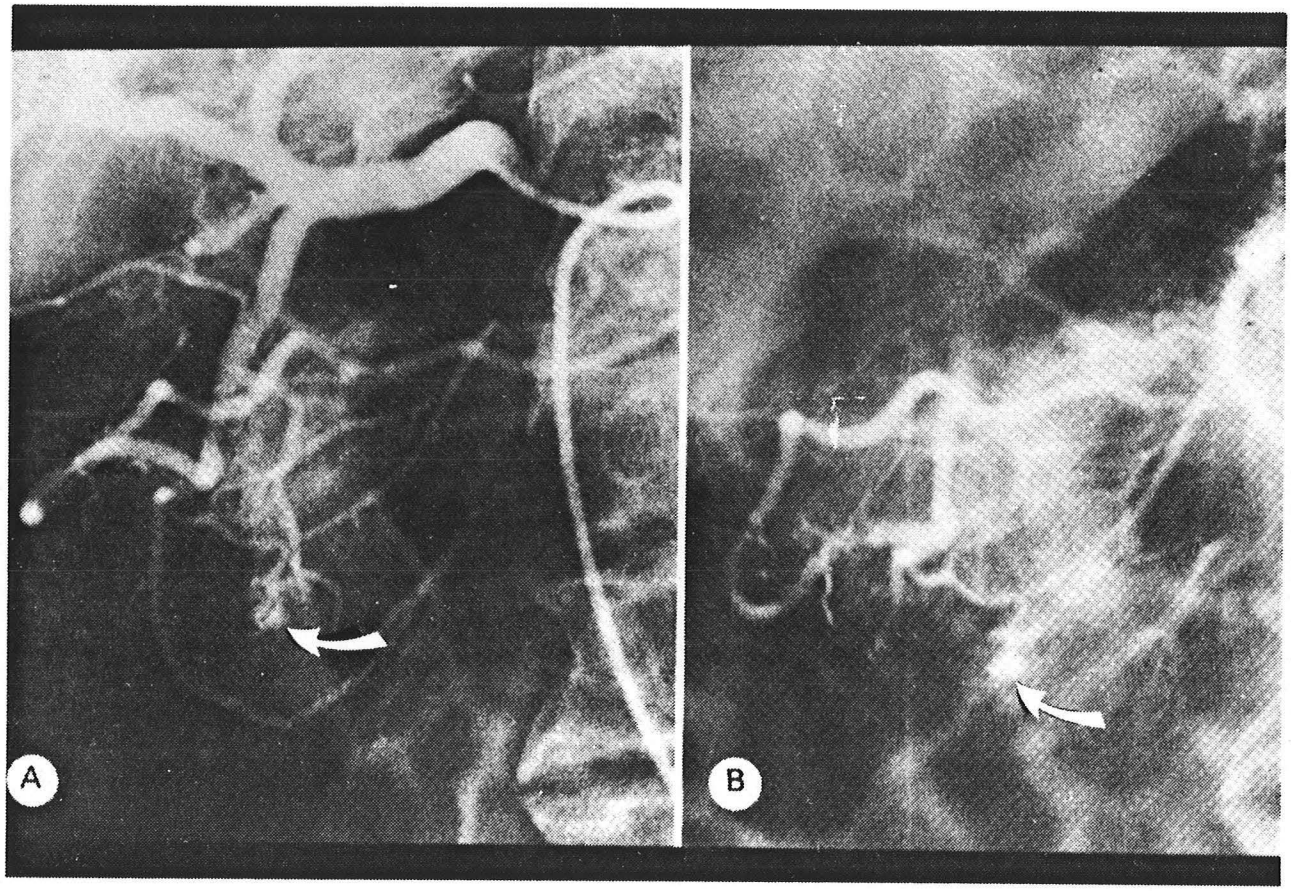
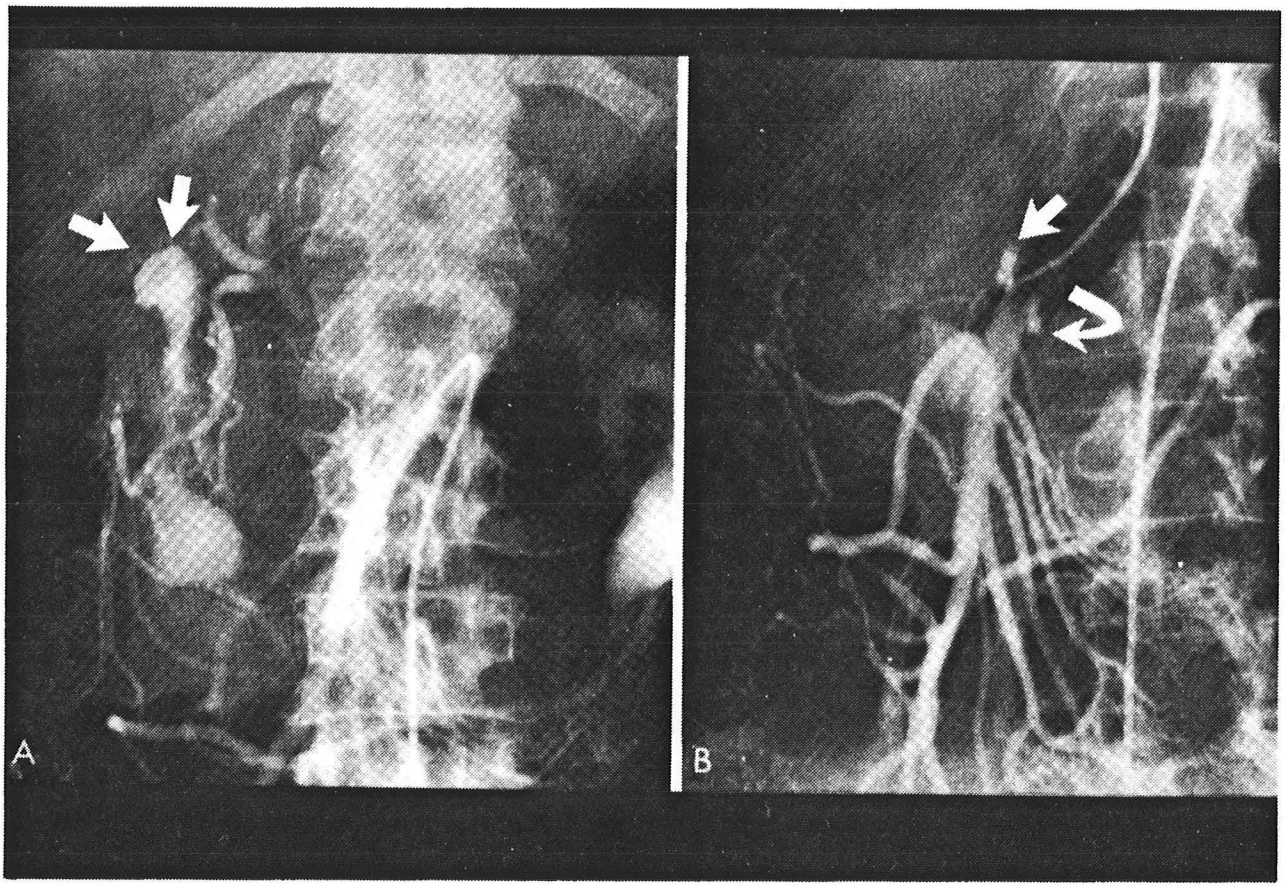
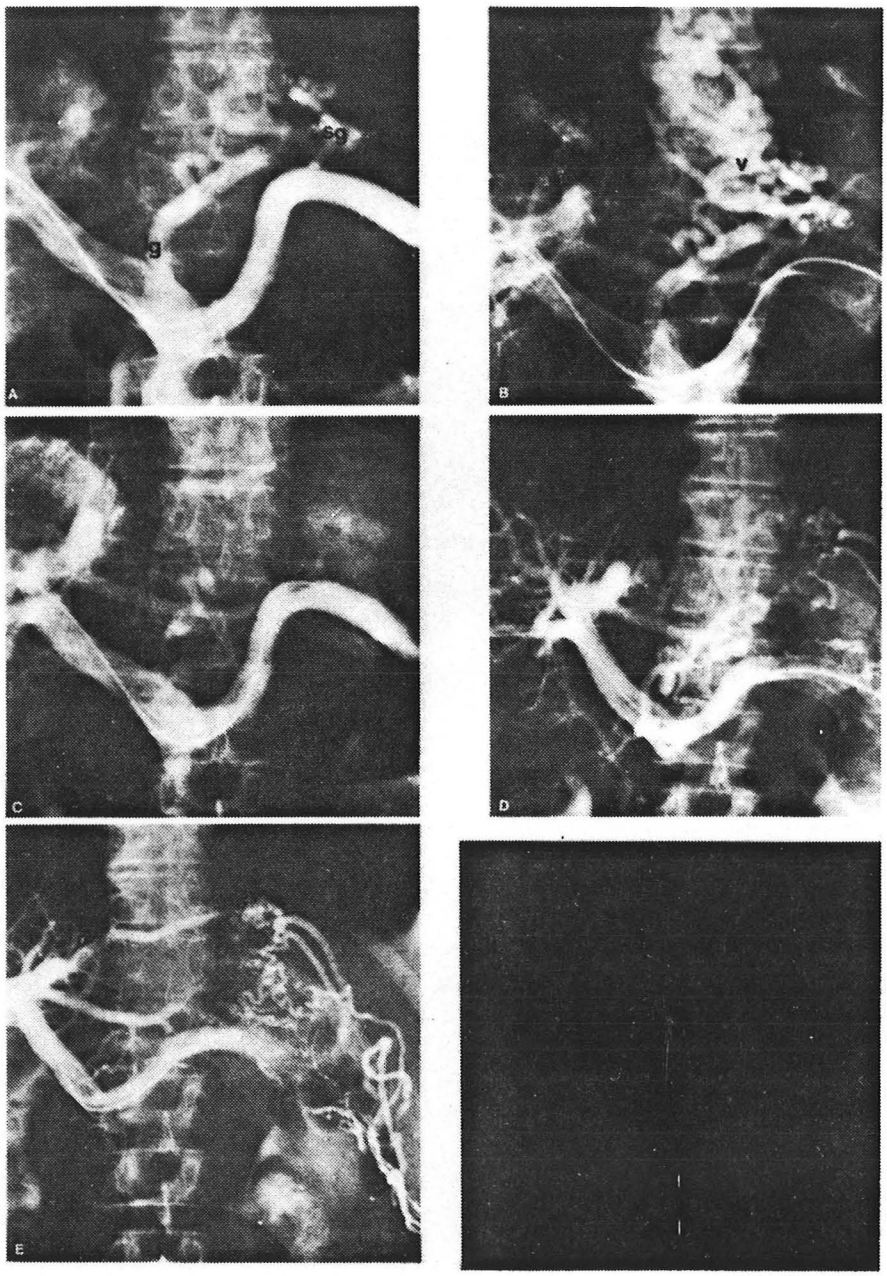
Bleeding duodenal ulcer. A, injection into hepatic artery demonstrating extravasation from small duodenal branch (arrow). B, injection into inferior pancreaticoduodenal artery demonstrating same branch as well as extravasation (arrow). Infusions into both limbs of arterial arcade may be necessary because of difficulty determining which vessel actually supplies bleeding point (From Ref. 79).



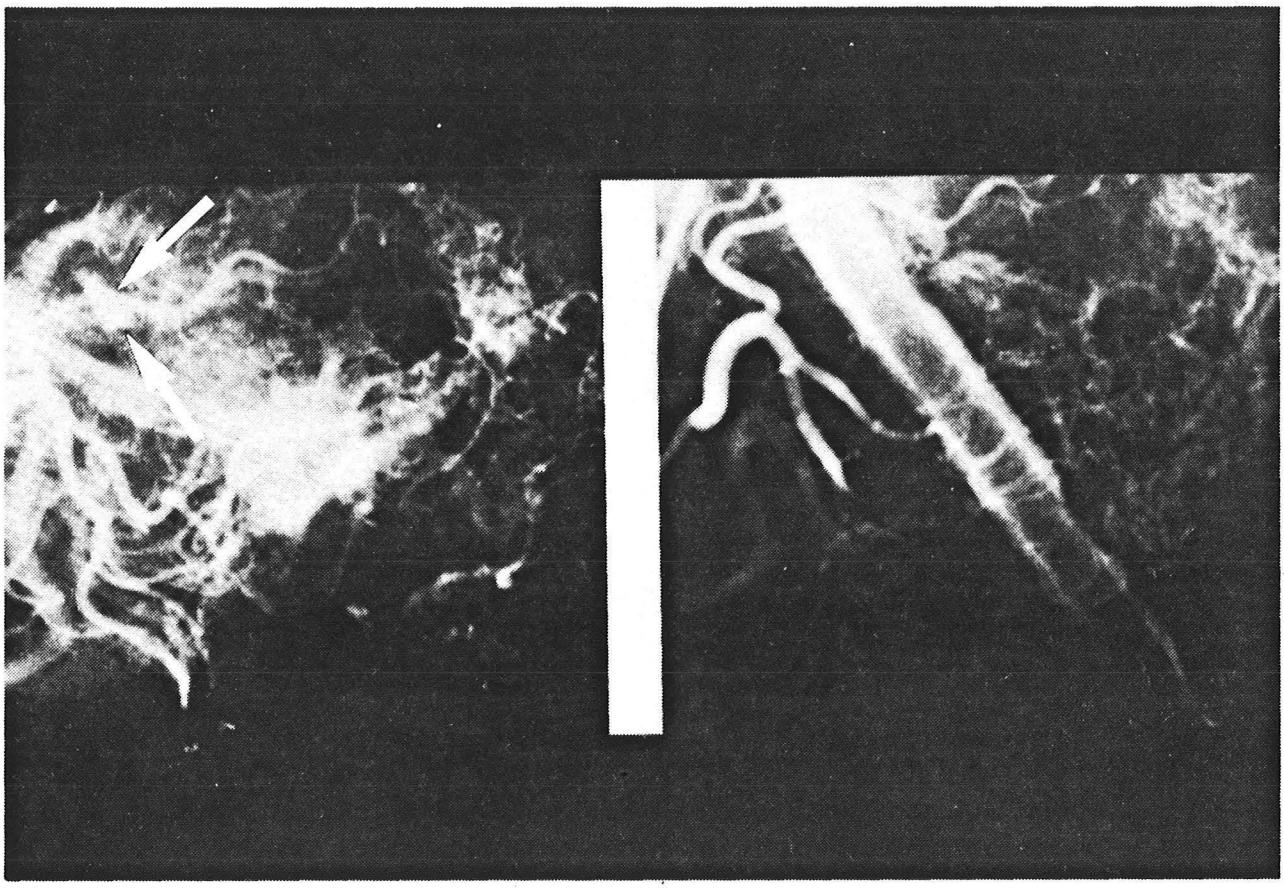
Bleeding from a duodenal ulcer controlled with transcatheter embolization. A, Superior mesenteric arteriogram shows retrograde filling of the gastroduodenal artery from the pancreaticoduodenal arcades and extravasation at the site of the bleeding duodenal ulcer (arrows). B, Sequential selective embolization of the posterior division of the inferior pancreaticoduodenal artery (straight arrow) and the anterior division of the same artery (curved arrow) was undertaken and the repeat superior mesenteric arteriogram shows effective obstruction of flow through the gastroduodenal artery and no extravasation (From Ref. 65).



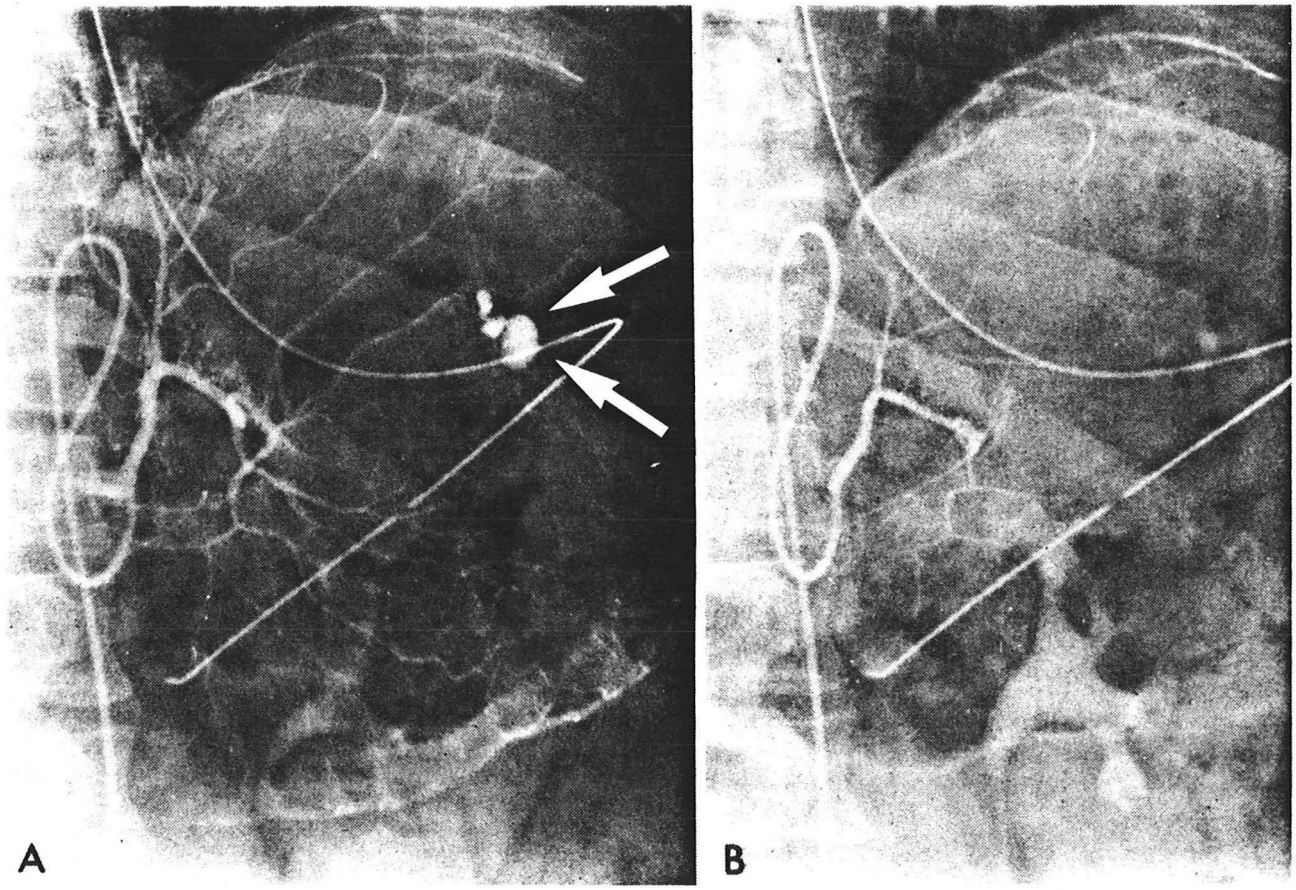
A. and B. Transhepatic portography demonstrates left gastric vein (lg) and short gastric vein (sg) supplying extensive varices (v). C. Following gelfoam injection both vessels fail to fill. D. Following further hemorrhage, transhepatic portography shows new variceal vessels which were then obliterated. E. Repeated variceal hemorrhage occurs from varices supplied by further development of new vessels. These proved impossible to obliterate (From Ref. 133).



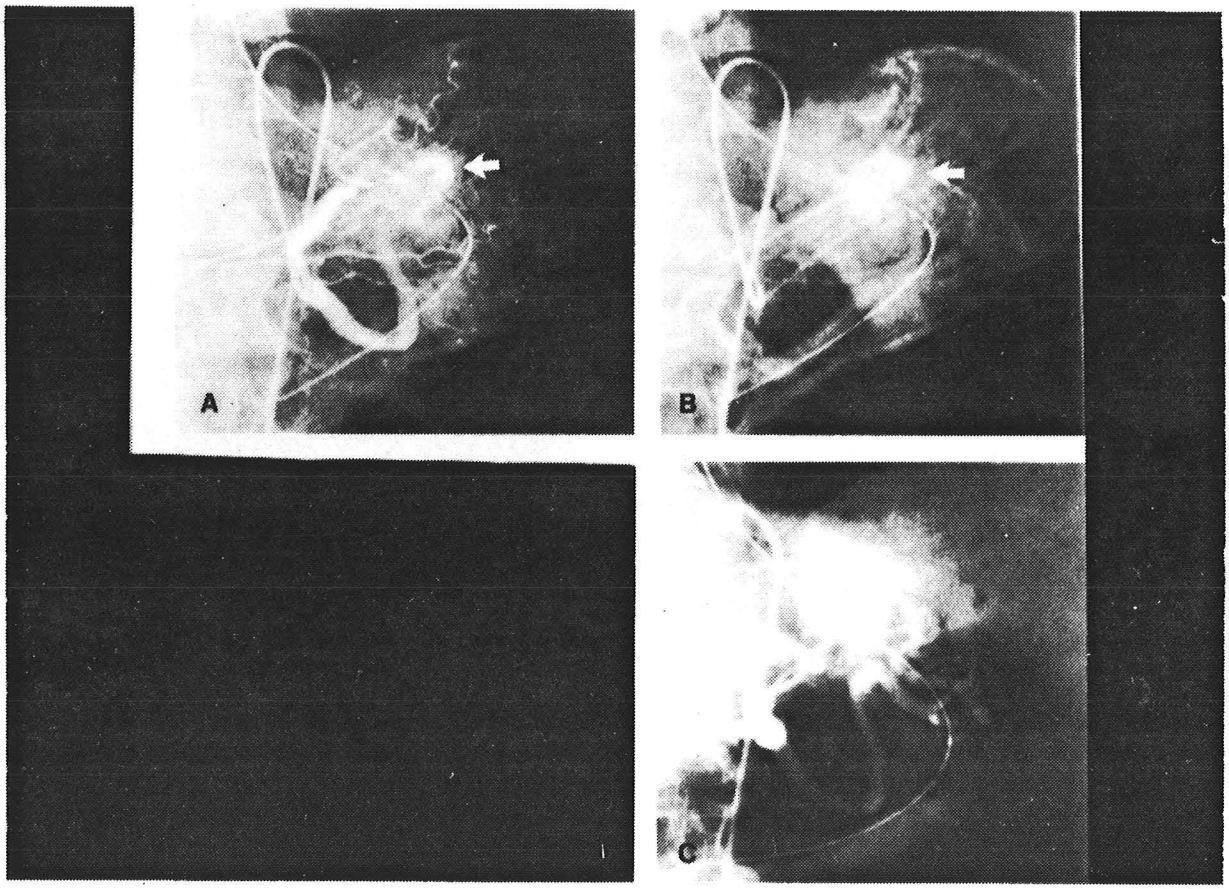
Left. Hyperemia and extravasation from Mallory-Weiss tear. Right. After vasopressin there is no extravasation (From Ref. 163).



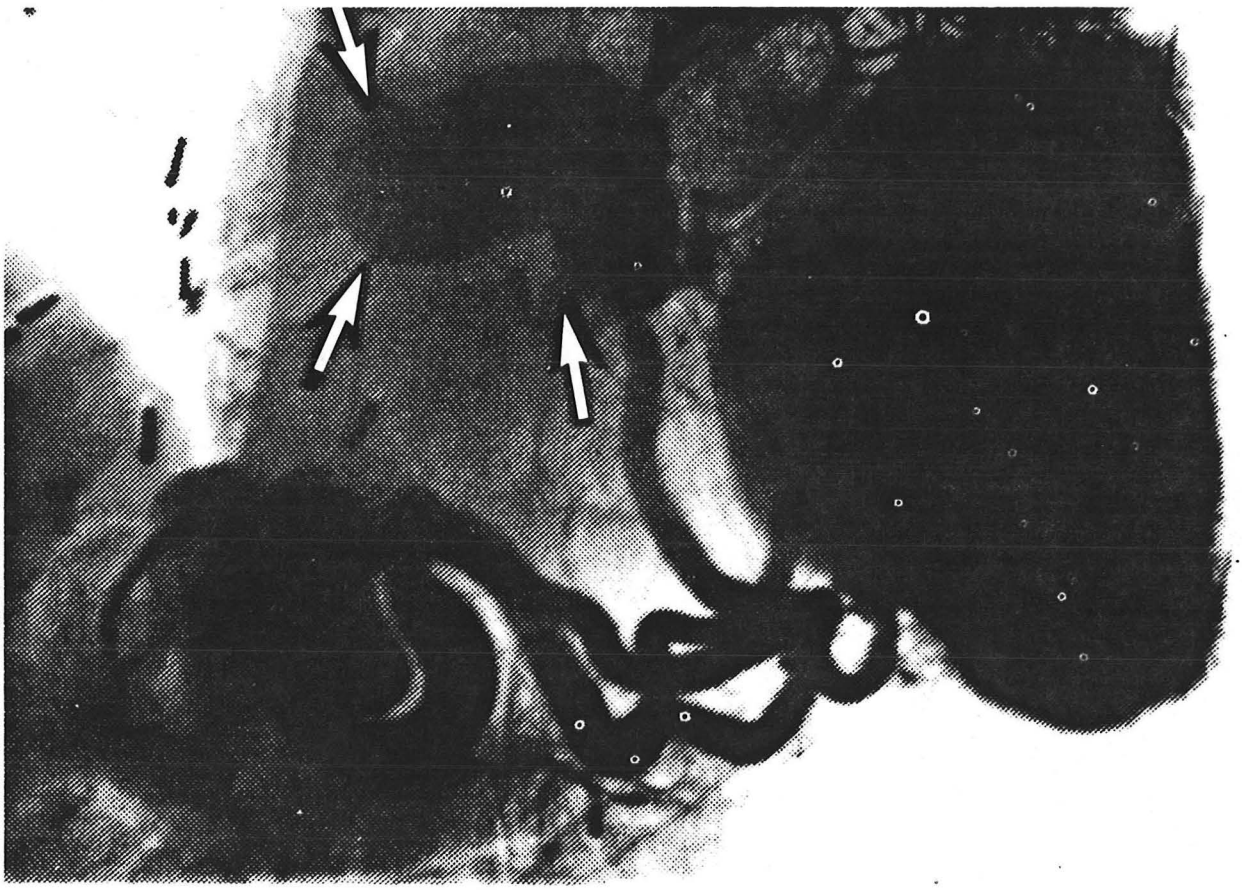
A, Selective left gastric arteriogram shows contrast extravasation in the gastric fundus (arrows). B, 20 minutes after vasopressin infusion at 0.2 U/minute in the left gastric artery, the arteriogram shows constriction of the branches of the left gastric artery and no extravasation (From Ref. 65).



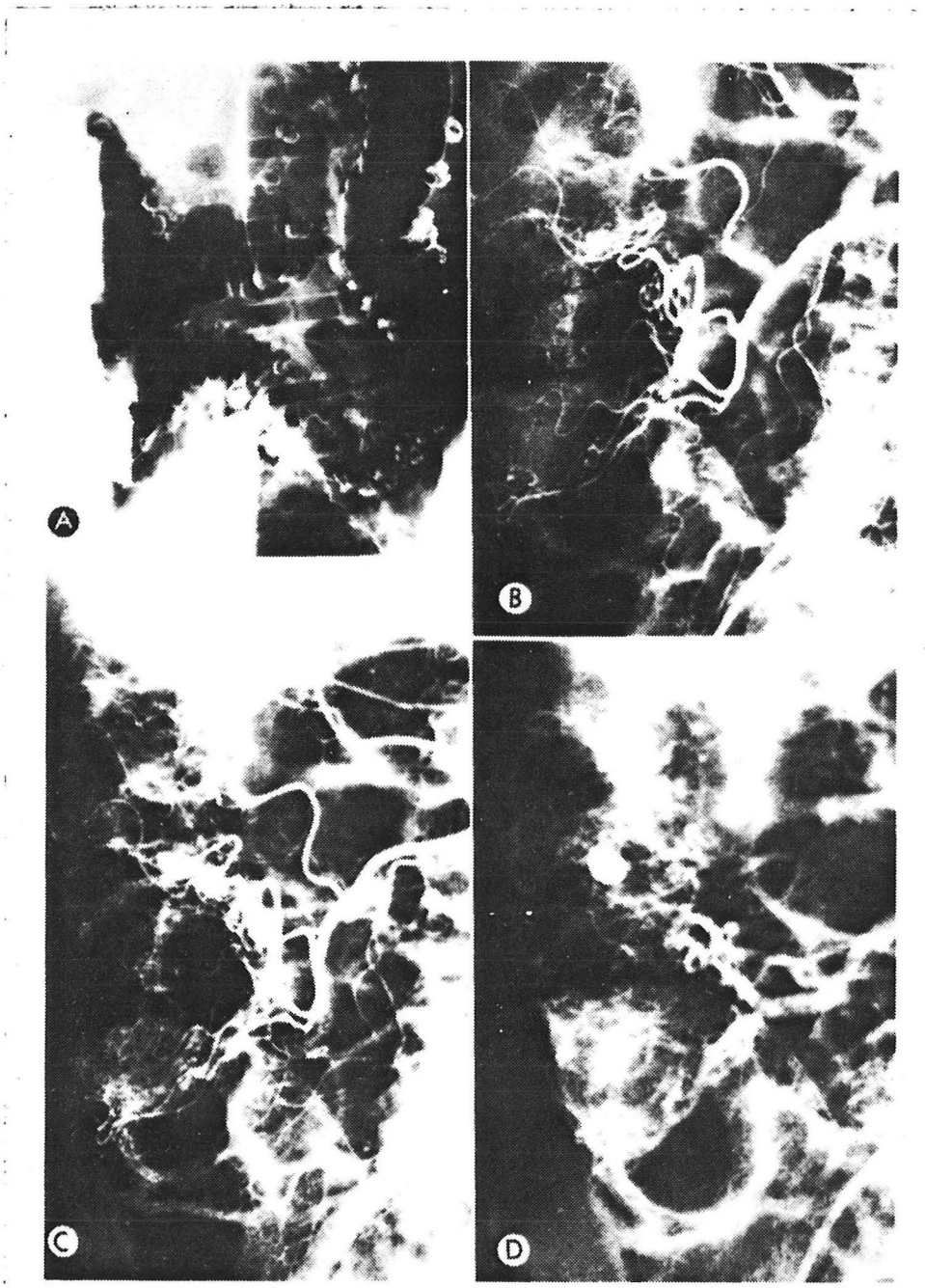
A, Arterial phase of left gastric artery injection showing extravasation in the proximal stomach (arrow) from gastritis. B, Venous phase of left gastric arteriogram showing accumulation of contrast material (arrow) in the proximal stomach. C, Control arteriogram following twenty minujtes of vasopressin infusion in the left gastric artery at a rate of 0.2 unit per minute shows no extravasation (From Ref 82).



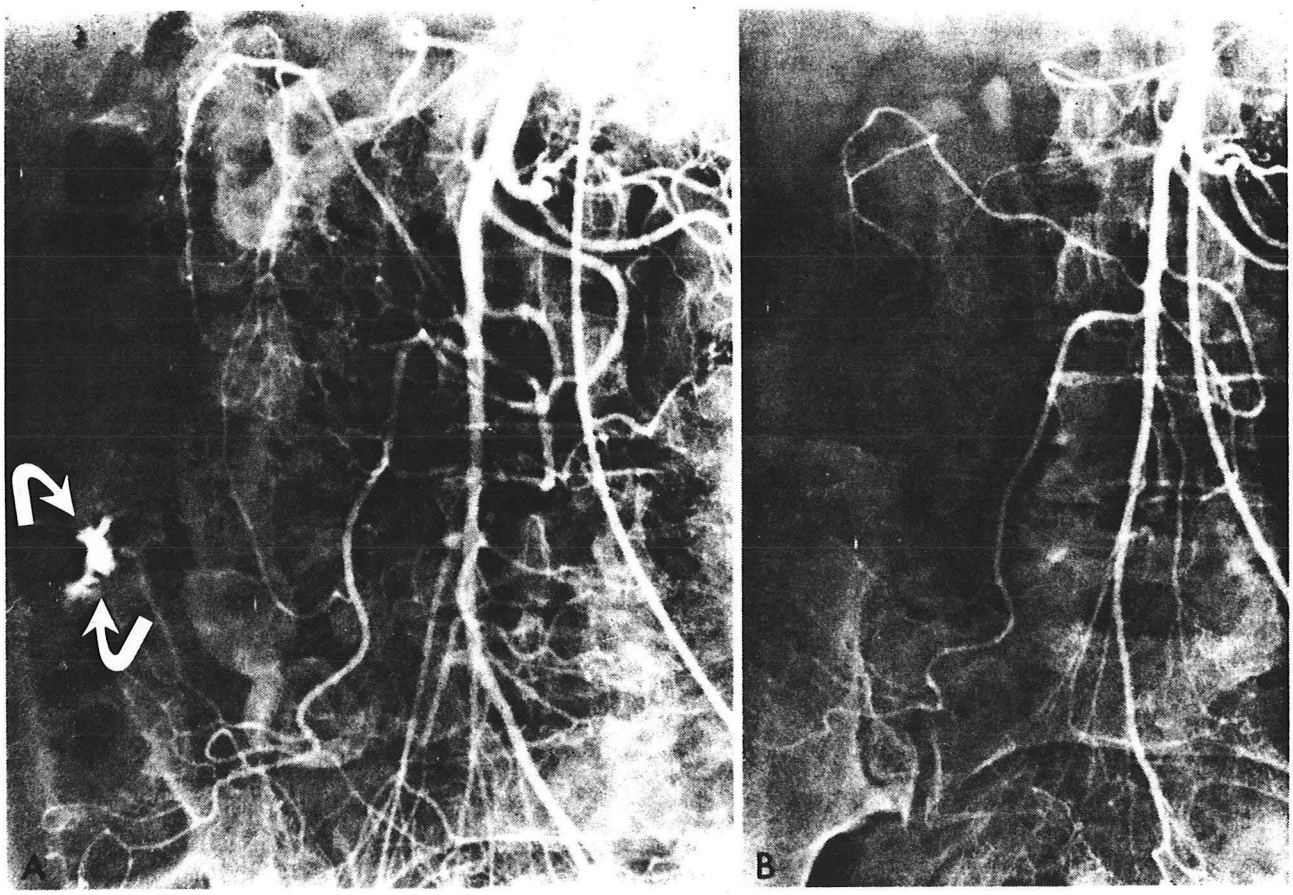
Aneurysm of splenic artery (From Ref. 178).



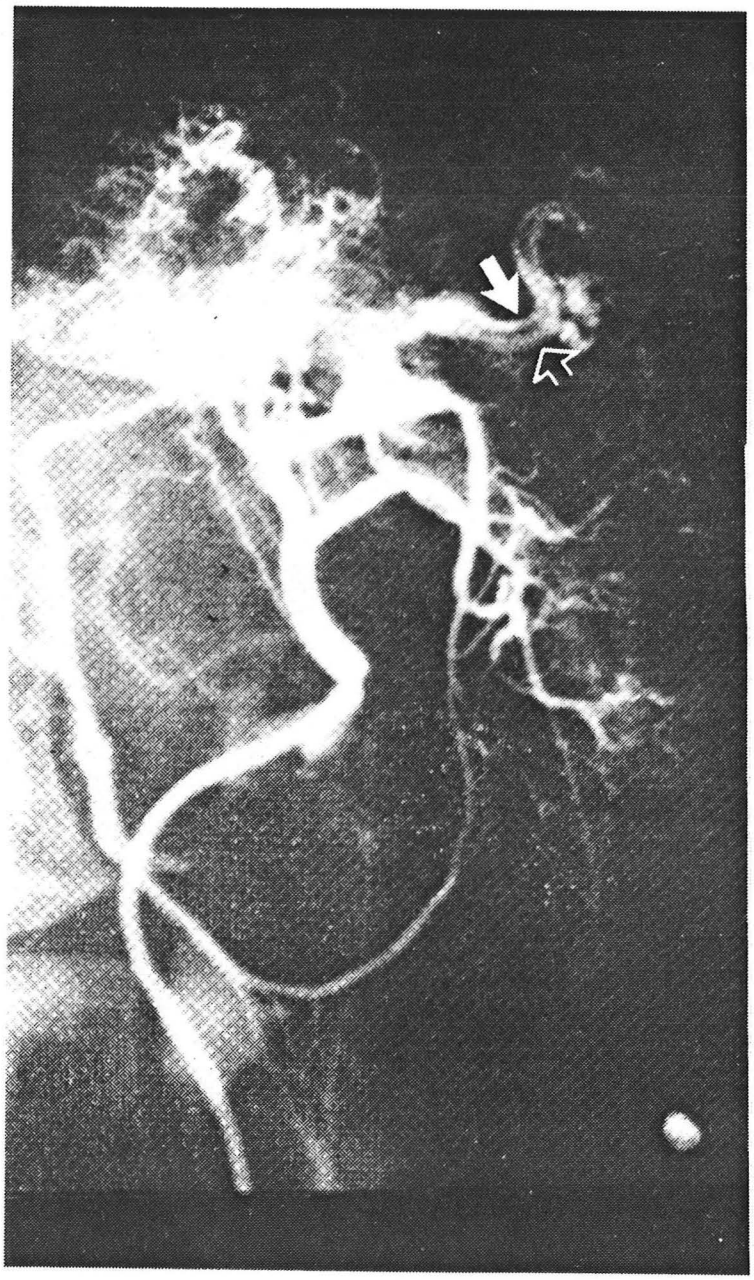
(A) A previous barium enema roentgenogram in a 67 year old man with acute rectal hemorrhage shows only a multiplicity of colonic diverticula. (B) Arterial and (C and D) venous phases of a superior mesenteric arteriography show the typical appearance of a bleeding colonic diverticulum. Contrast material extravasates into the diverticulum and pools within it, revealing a persistent, sharply marginated density throughout the venous phase (From Ref. 190).

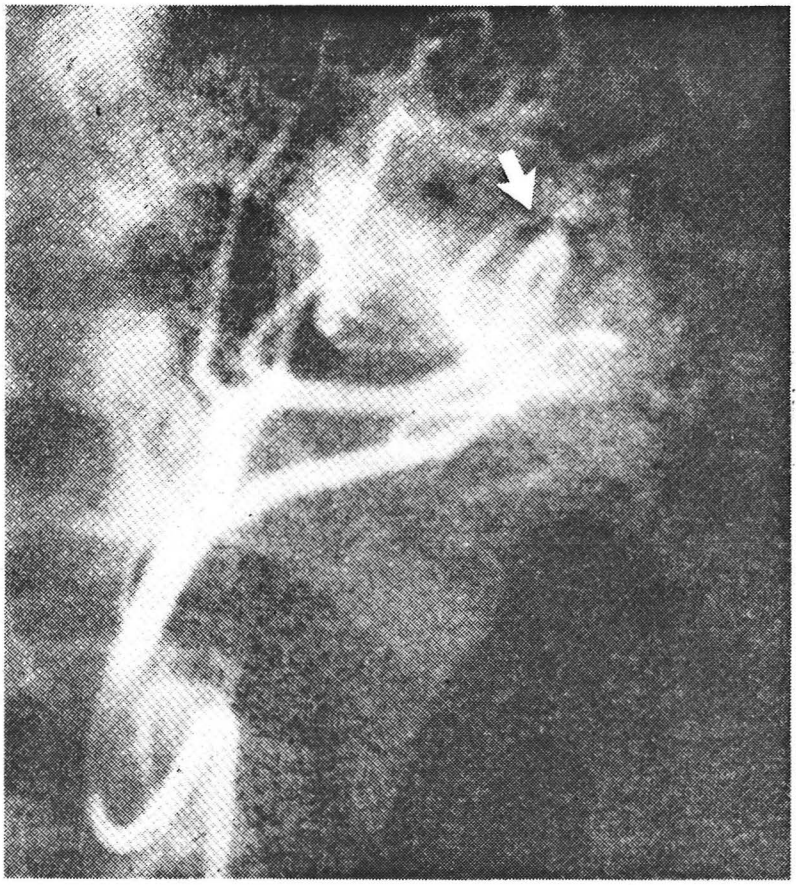


Massive bleeding from diverticulum of the right colon controlled with vasopressin infusion into the mesenteric artery. A, Superior mesenteric arteriogram shows extravasation in the ascending colon (arrows) from a branch of the ileocolic artery. B, Repeat mesenteric arteriogram after 20 minutes of vasopressin infusion at 2 U/minute into the mesenteric artery shows constriction of the mesenteric arterial branches and no extravasation (From Ref. 65).

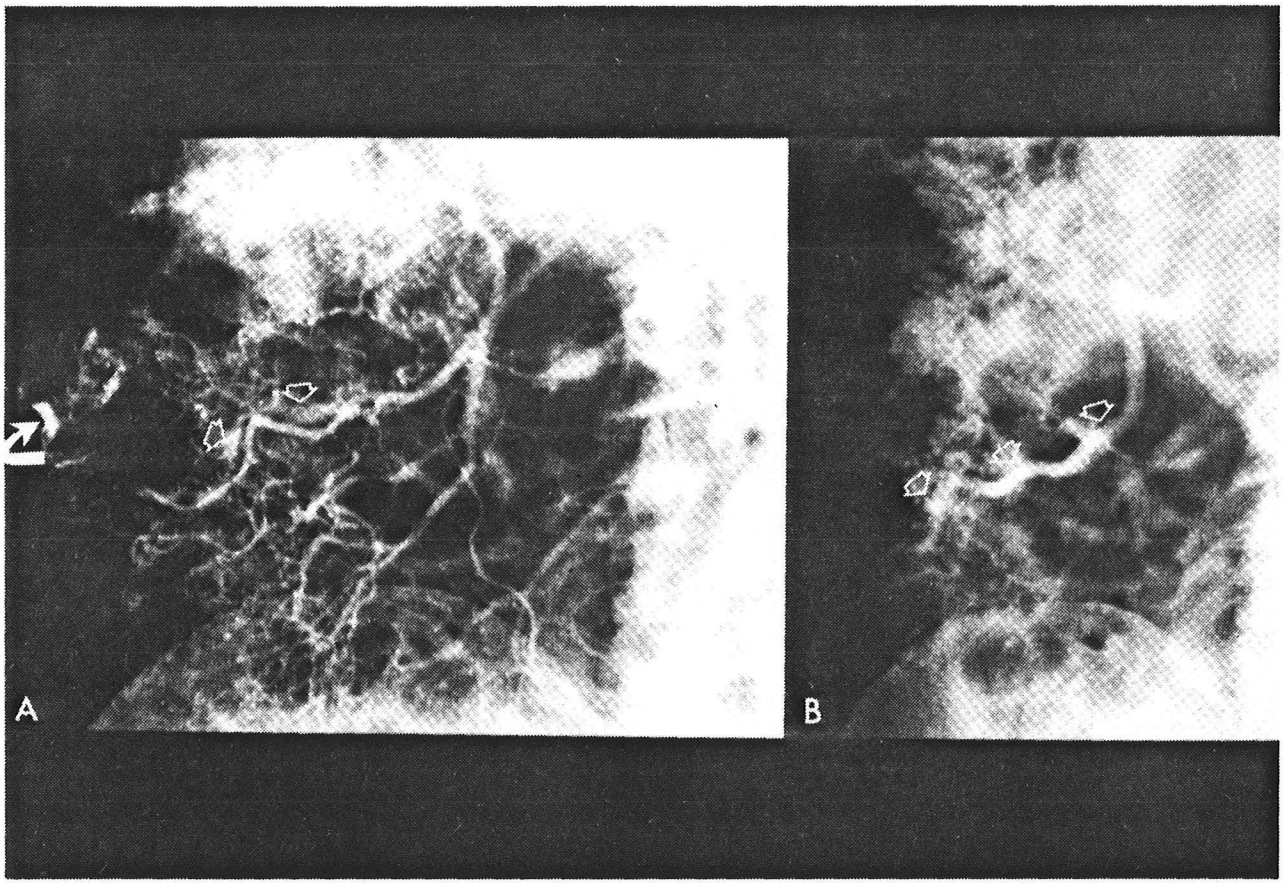


Arterio-venous malformation. (Left) Oblique view of selective left gastric arteriogram shows simultaneous opacification of the artery (arrow head) and vein (open arrow) (Right) Postembolization left gastric arteriogram shows complete occlusion of the secondary branch of the left gastric artery (arrow) and the malformation is not seen (Ref. 239).

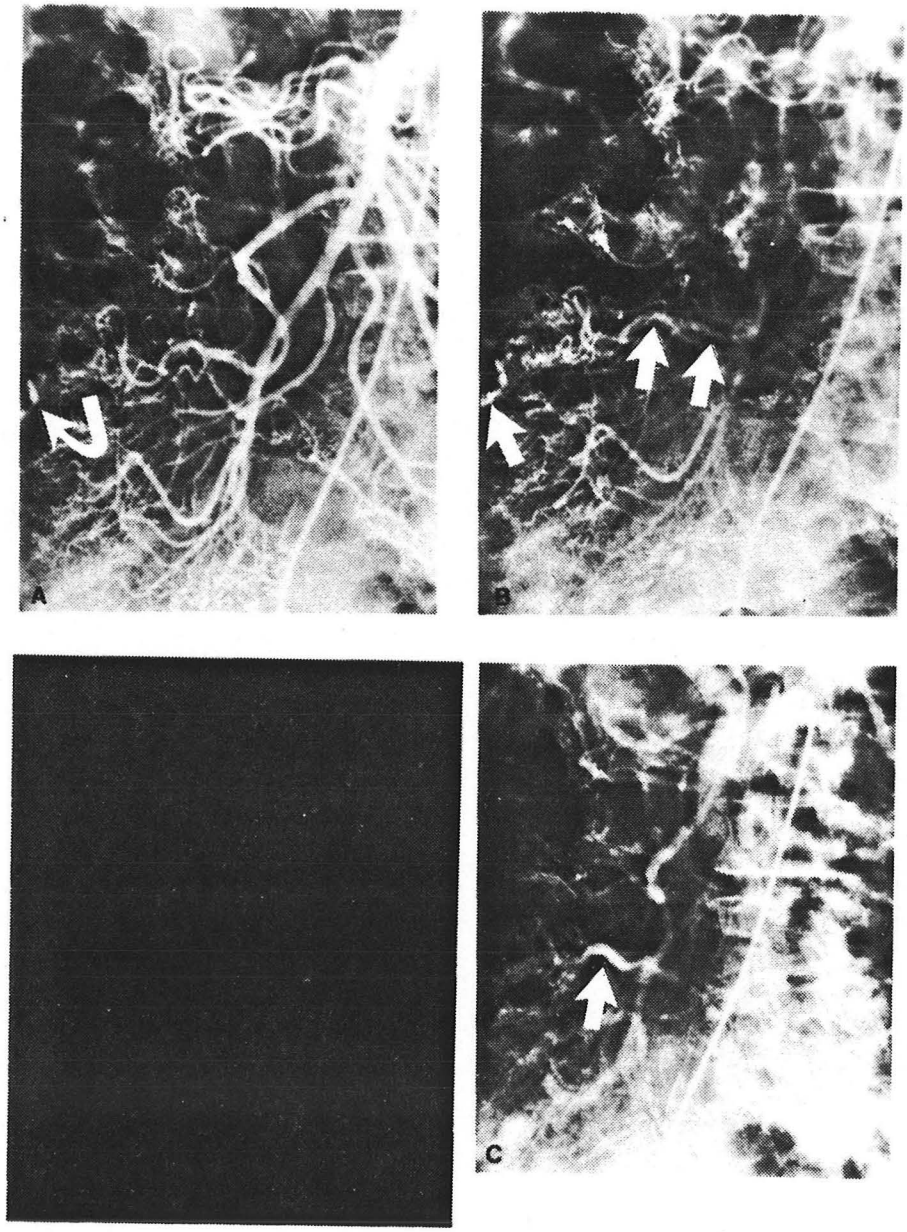




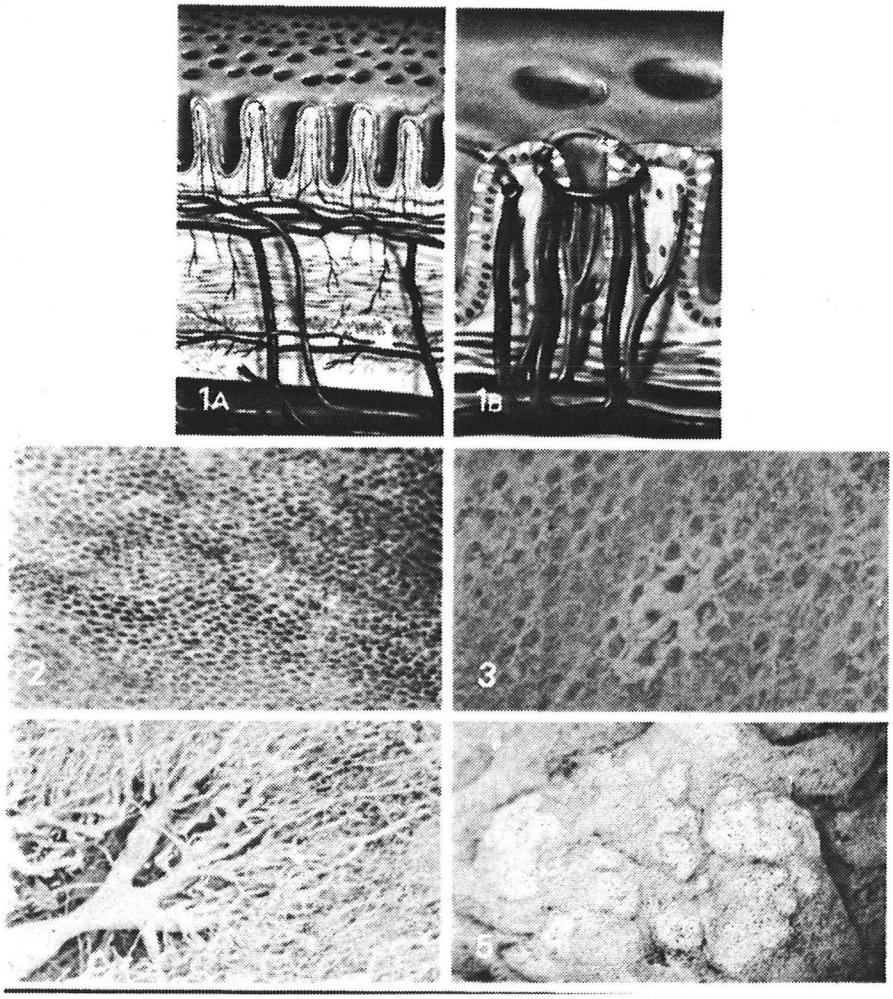
Vascular ectasia of the ascending colon. Colonoscopy and barium enema examinations were unrevealing. A, The arterial phase of a superior mesenteric arteriogram shows accumulation of contrast medium in a vascular space along the antimesenteric border of the ascending colon (curved arrow) and early opacification of a draining vein (straight open arrows). B, During the late phase of the mesenteric arteriogram there is persistent intense opacification of the same draining vein (arrows) (From Ref. 65).



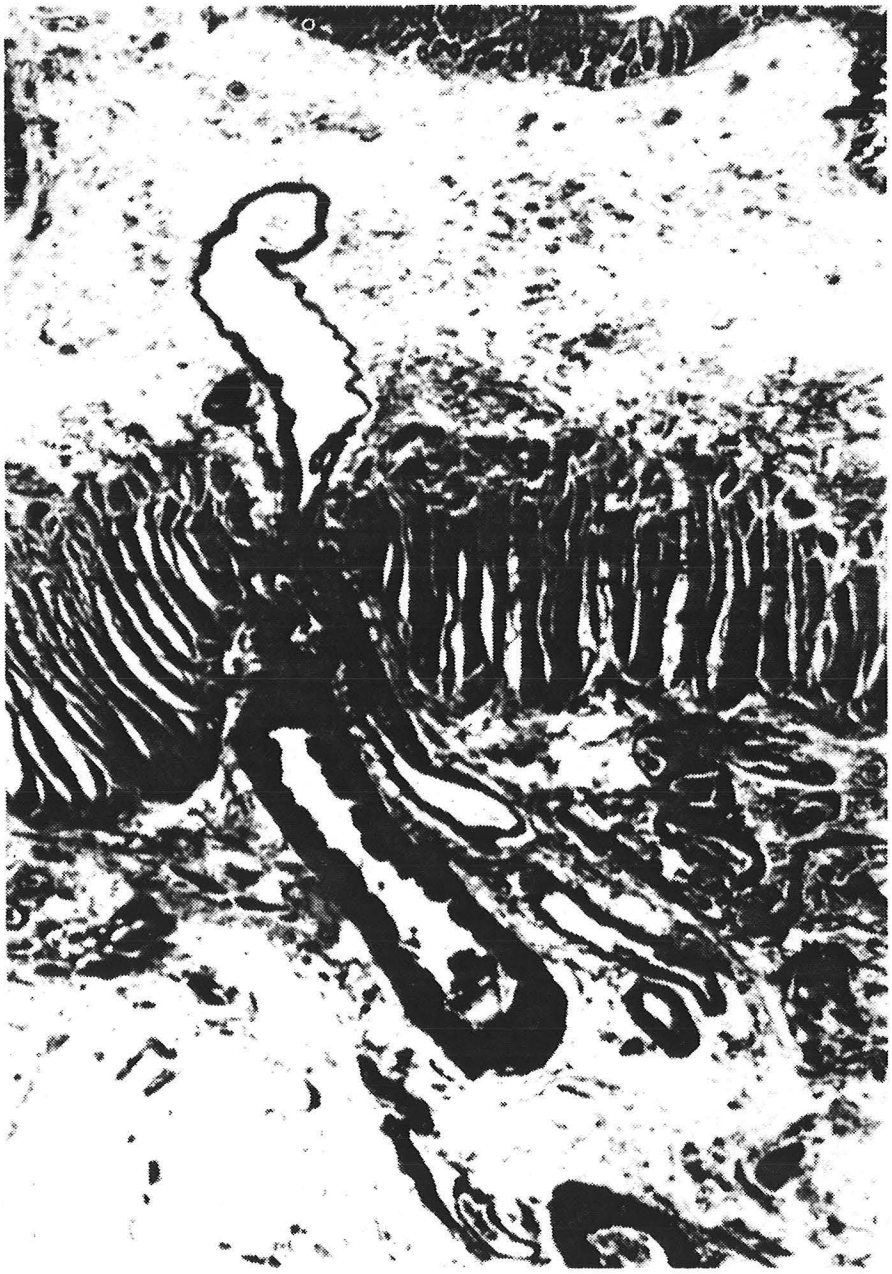
Colonic angiodysplasia. A, Superior mesenteric arteriogram shows a vascular tuft (curved arrow) in the antimesenteric border of the cecum. B, During the late arterial phase, the vascular tuft (straight arrow) and an early draining vein are noted (arrows). C, During the venous phase there is intense opacificaiton of the draining vein (arrow) (From Ref. 243).



1.A, vascular anatomy of colonic wall. The vasa recta and brevia and their accompanying veins penetrate the circular and longitudinal muscles to form the submucosal plexus. Branches from this plexus then go to the mucosa and muscular layers. B, arteriolar-capillary-venular unit of colonic mucosa.
2. Normal "honeycomb" pattern of the mucosa in injected and cleared specimen. The pattern is formed by the capillary rings surrounding the crypts of the mucosa.
3. Minimal mucosal ectasia involving only a few surface capillary rings with normal pattern in the surrounding mucosa.
4. More extensive ectasia involving many capillaries. Dilated veins communicating with the submucosa are clearly seen.
5. Group of mucosal ectasias which all communicate with one large submucosal vein. (From Ref. 244).

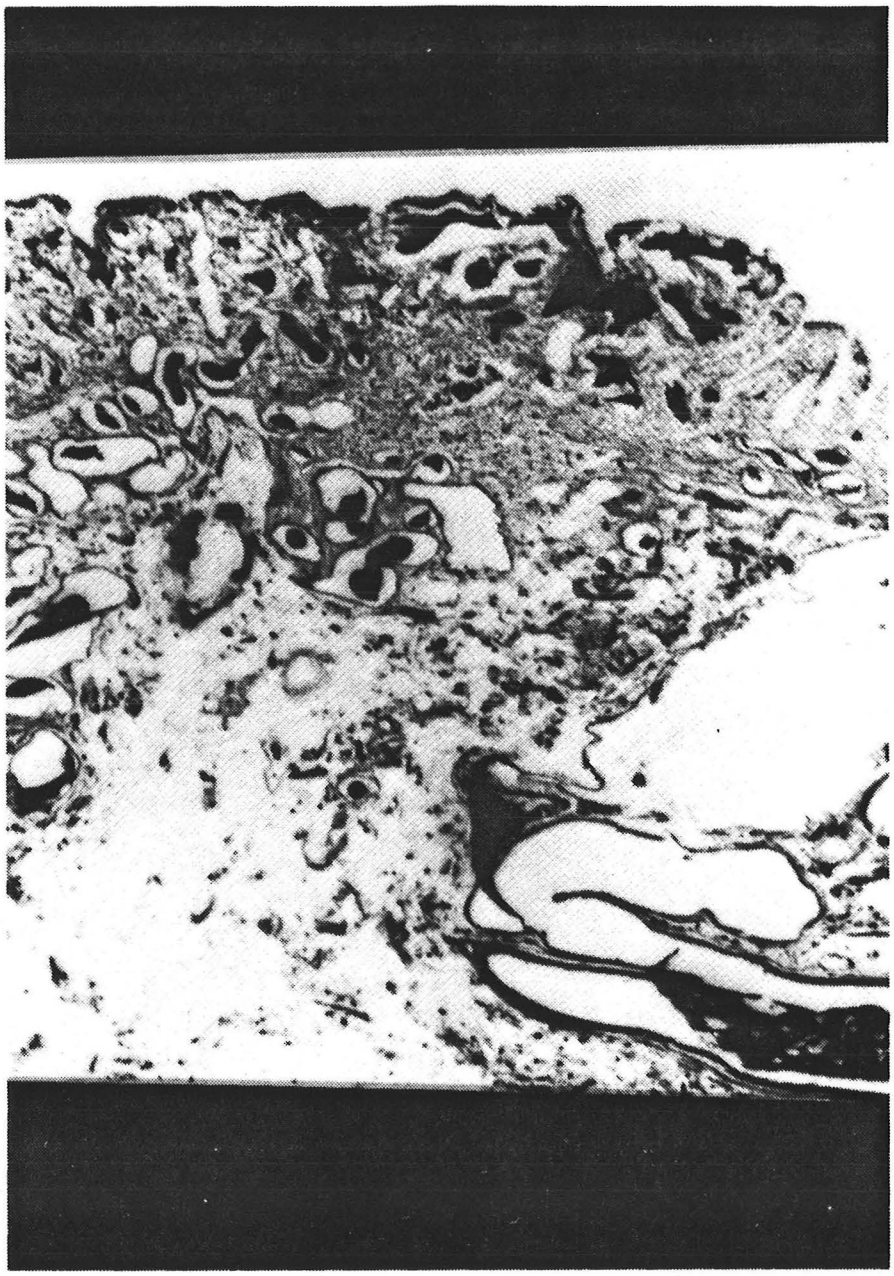


Vas recta and accompanying vein traversing the cecal muscle layers. The compression of the vein is the functional anatomic explanation for the intermittent, partial, low grade venous obstruction producing vascular ectasias (From Ref. 244).



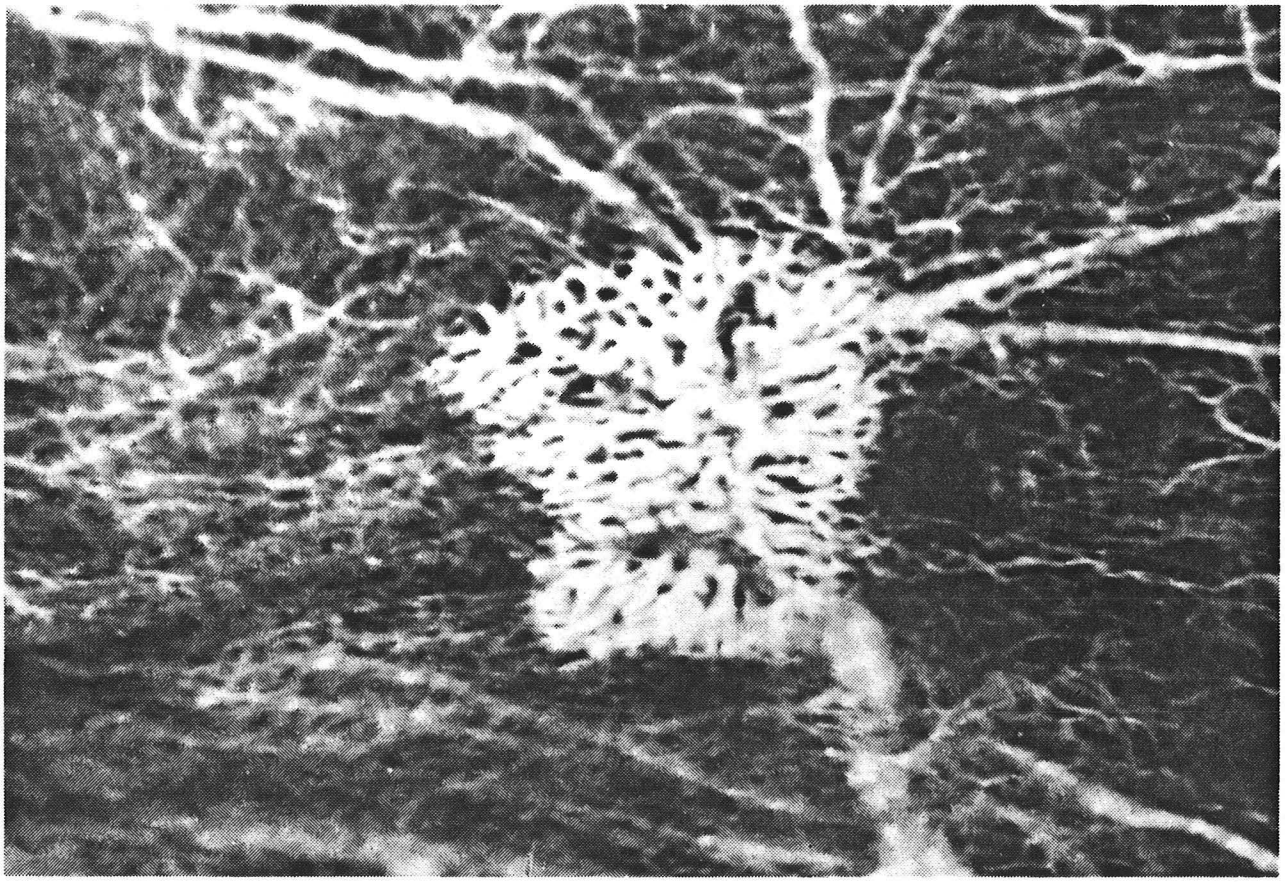
Injected and cleared specimen viewed with transillumination and showing the prominent dilated and tortuous submucosal vein draining a small area of mucosal ectasia (arrows). An artery of normal caliber is seen in the lower left corner (From Ref. 237).

Early stage of angiodysplasia. Dilated tortuous submucosal veins extending through the muscularis mucosae and continuous with a few dilated venules and capillaries in the mucosa. Black material in vessels is injected Microfil (From Ref. 237).



Late stage of angiodysplasia. Higher magnification of end stage ectasia demonstrating loss of mucosal supporting structures and glands. Only the thin wall of the vessel separates the vascular lumen from the bowel lumen (From Ref. 237).

Angiodysplasia lying astride a submucosal vein (From Ref. 243).



Scanning electron microscopy. (A) A vascular ectasia is seen projecting above the normal surrounding mucosa. In the lower half of the lesions exposed dilated vessels are seen in areas without surface epithelium. (B) Exposed dilated and distorted surface vessels which on cross section (D) are seen to be venules and capillaries. (C) High magnification showing abnormal dilate vessels with an apparently normal vessel entering them (arrows). (D) Cross section showing markedly dilated veins (V) in the submucosa and replacement of the mucosa by tortuous venules (vv) and capillaries (c); there is a paucity of arterioles (From Ref. 237).