MEDICAL GRAND ROUNDS

Southwestern Medical School

Dallas, Texas

UPPER GASTROINTESTINAL HEMORRHAGE

The Problem

The Causes

The Surrounding Circumstances

The Diagnosis

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Gastric Lavage and Cooling
Intra-gastric Vasoconstrictor
Sengstaken-Blakemore Tube
Vasopressin
Gastric Neutralization
Endoscopy

Selected References

Walter Peterson, M. D.

January 6, 1977

Case #1

"Ulcer occurring in the small part of the stomach. First hemorrhage healed; second hemorrhage fatal. Opening of the coronary artery of the stomach.

Little fellow, twenty-nine years, carpenter, sanguine temperment, muscular, since childhood given to the use of liquor. Five years ago he had large hemorrhages every evening for eight days which yielded to astringents. Two months of repose in bed were necessary for the patient to recover. His strength returned to him, he went back to his labor and again to his bad habit without his health appearing to suffer noticeably.

April 15, 1830, burning and pain in the epigastrium; loss of appetite. He was able however to continue his work until the evening of the 30th when general malaise forced him to go to bed. Immediately afterwards, vomiting of blood in a quantity perhaps of five or six pints. Carried to the Charite he showed a small pulse, compressible, an anemia almost complete which prohibited the idea of bleeding; we gave him then sinapisms to the feet.

The first of May, the patient vomited only once a small amount of blood, his pulse revived with his strength. (Twenty leeches to the epigastrium, sinapisms to the calves, rice mixed with eau de Kabel and syrup of quince; emulsion with the syrup of diacodium; diet.) In the evening, a large hematemesis.

The second of May, same condition, no stools. (Twenty leeches to the anus, sinapisms; same drink.) At five in the evening, hematemesis more marked than the preceding ones, extreme prostration; death at ten o'clock.

Opening of the Body--Skin discolored, marked adiposity. The abdomen opened, we are struck by the purplish red color of the large intestine, which contrasts with the pallor of the stomach and of the small intestine. The stomach contains a bloody fluid in which several clots swim. At the level of the lesser curvature there is a deep ulceration, circular, six lines in diameter, circumscribed by a very dense margin. The edge and floor of the ulcer are cicatrised, excepting where there is a clot of blood elevated like a nipple."

From Cruveilhier,J. Anatomie pathologique du corps humain 1830-1842.

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Case #2

R.M., a 22 year old man, presented to the Parkland Memorial Hospital emergency room after being shot through the abdomen. At laparotomy a bleeding liver laceration was sutured and his post-operative course was uneventful. Three days after discharge he developed right upper quadrant pain and was admitted with jaundice, a hemoglobin of 9.7, and elevated liver enzymes.

Nasogastric aspiration revealed bloody material and he was treated for an UGI bleed. When he continued to bleed, endoscopy was performed disclosing blood spurting from the Ampulla of Vater. Celiac arteriography was then performed and demonstrated a 5.5 cm rounded filling defect in the right hepatic lobe. An arteriobiliary fistula was seen at the edge of this defect and clots were present in the biliary tree. Bleeding had ceased. He was treated conservatively, did well, and a repeat arteriogram four weeks later showed a marked decrease in the size of the filling defect and no arteriobiliary communication. Four weeks later a final study was normal.

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These two cases of upper gastrointestinal hemorrhage differ more than in the style of the text. Cruveilhier lacked the sophisticated diagnostic procedures employed in the second case and was forced to rely on what we might term crude therapeutic means. Endoscopy and angiography represent but two of the modern day advancements used in the diagnosis and treatment of UGI bleeding. This discussion will examine how good they are and what role they play in the context of other modalities employed to diagnose and treat upper gastrointestinal bleeding today.

The Problem

Literally thousands of articles have been published about UGI bleeding over the past ten years. Rather than present a complete compendium of statistics from other sources, this discussion will use the literature to establish trends against which the experience at the Dallas VA Hospital will be recounted. Data from other institutions is so subject to the variabilities of patient selection, diagnostic approaches, and surgical bias as to render any other approach futile. Table 1, then, displays the experience for one year (1975) from the DVAH.

Table 1

DVAH - 1975

Total consults to gastroenterology:	1210
G-I bleeders:	145
U-G-I bleeders:	100

Age		Mortality
---	Literature	10%
55 yrs.	DVAH	20%

The Causes

The causes of UGI bleeding are legion but for convenience can be categorized as follows:

1. Ulcerating Lesions
   a. *Esophagitis* -- rare sequel of gastroesophageal reflux; other symptoms usually antedate bleed; can be massive; usually responds to medical management (7).

   b. *Acute Gastric Mucosal Lesion*-- superficial lesion (gastritis); associated with stress, aspirin, and ? alcohol; mechanism involves back diffusion of hydrogen ions through a broken mucosal barrier (8-11).

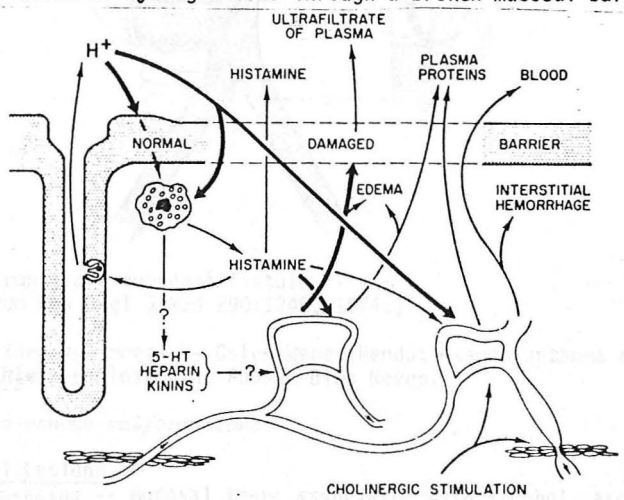

Figure 1. Results of damage to gastric mucosal barrier. (From Davenport, H. Gastroenterology 50:487, 1966.)

   c. *Gastric Ulcer* -- older patients; may be associated with aspirin ingestion; may be asymptomatic.

   d. *Duodenal Ulcer* -- may be asymptomatic; occurs in 15-20% of patients with ulcer.

2. Vascular Lesions
   a. *Varices* -- may occur throughout GI tract; associated with severe liver disease and portal hypertension; often present but not cause of bleeding (12,13).

   b. *Arterial-enteric fistula* -- usually an aneurysm but may be inflammatory invasion; almost any vessel may be involved; a surgical emergency.

c. *Dacron graft-enteric fistula* -- diagnosis in such patients until proven otherwise; usually erodes into duodenum; knitted dacron and plastic sutures have decreased incidence (14,15).

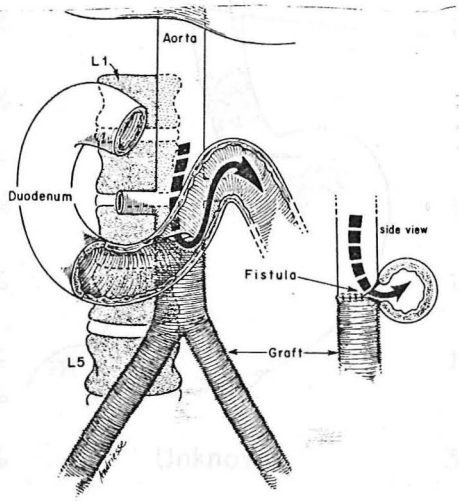

Figure 2. Dacron graft-duodenal fistula.
(From New Engl J Med 290:1248, 1974.)

d. *Hereditary syndromes* -- Osler-Weber-Rendu; Pseudoxanthoma elasticum; Ehlers-Danlos; Blue Rubber Bleb Nevus.

e. *Arterio-venous malformations*

3. Mechanical Lesions
   a. *Mallory-Weiss* -- mucosal tear; associated with alcohol, aspirin, or both in 90%; preceded by retching; usually in the stomach; rarely fatal; responds to medical management (16-18).

   b. *Hemobilia* -- associated with trauma or aneurysm; often associated with pain and jaundice; may be pancreatic (19).

4. Tumors -- *Carcinoma; Lymphoma; Leiomyoma; Polyps; Sarcoma; Neurofibroma.*

5. Systemic Diseases -- *Blood dyscrasias; Connective Tissue Disorders; Uremia.*

Figure 3 compares the causes of UGI bleeding at the Dallas VA Hospital with average results from the literature.

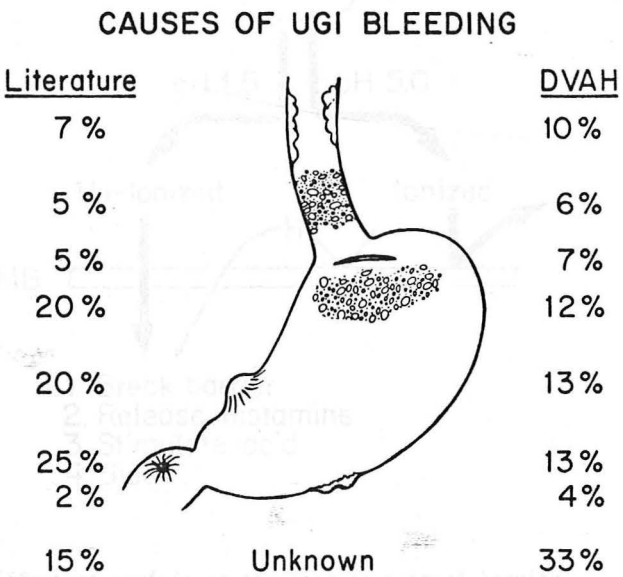

Figure 3. Causes of UGI Bleeding: Literature vs DVAH.

The Surrounding Circumstances

A number of factors have been mentioned in the literature as either predisposing an individual to UGI bleeding or, once the hemorrhage has occurred, adversely affecting the chance for survival. Several drugs with anti-inflammatory actions have been indicted as predisposing to UGI bleeding. These include aspirin, indomethacin, butazolidin, and corticosteroids. Convincing controlled data is unavailable to support the validity of these claims for all but aspirin (20). Indeed, Conn has concluded that there is a definite non-association of corticosteroids and peptic ulcer (21). Careful thought, however, must be given to readministering any drug to a patient who has bled in the past while taking that particular drug.

Davenport originally demonstrated the effect of *aspirin* on the gastric mucosa (22). In studies using dogs, aspirin broke the gastric mucosal barrier allowing the back diffusion of hydrogen ions from the gastric lumen. Bleeding soon ensued. Buffered aspirin failed to do this, even when alcohol was added. Since aspirin is a weak acid with a pKa of 3.5, higher pH levels will leave the drug in an ionized form. It is postulated that this form, being relatively lipid insoluble, will not diffuse into the mucosal cell and, therefore, be unavailable to exert its damaging influence (Figure 4).

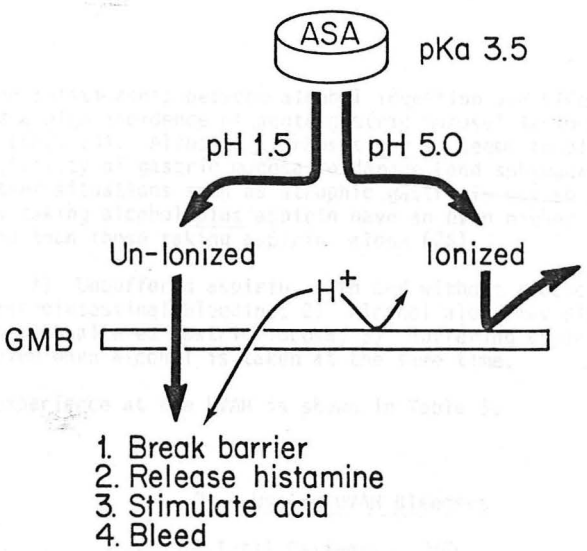

Figure 4. Effect of aspirin on the gastric mucosal barrier.

Studies in humans confirm this hypothesis. Normal healthy males lose 0.4 ml of blood in the stool each day (23,24). With regular aspirin, this increases to 3.2 ml per day (23) while buffering the aspirin will prevent an increased blood loss, even when given with alcohol (24). Although clinical studies in patients with UGI bleeding are often criticized for lack of adequate control groups, at least three show that aspirin use is far higher in patients who bleed compared to those who do not (25-27)(Table 2).

Table 2.

Aspirin Use in Bleeders

	Control	Bleeders
Percent Using Aspirin:	7-32%	16-75%

Aspirin predisposes individuals to UGI bleeding from acute gastric mucosal lesions and gastric ulcer but has no relationship to either uncomplicated or bleeding duodenal ulcer (25).

Alcohol also breaks the gastric mucosal barrier (29) but in normal subjects does not by itself induce excess daily blood loss (23,30). Only alcoholics with atrophic gastritis appear to bleed with alcohol ingestion (30). In all cases, however, alcohol will heighten the blood loss occurring with unbuffered aspirin (23). Clinical studies of UGI bleeders are conflicting.

Some find no relationship between alcohol ingestion and bleeding (26) while others find a high incidence of acute gastric mucosal lesions in bleeders imbibing alcohol (9). Although cirrhosis per se seems to play no part in the susceptibility of gastric mucosa to damage (and subsequent bleeding) by alcohol, other situations such as atrophic gastritis may so predispose. Individuals taking alcohol plus aspirin have an even higher incidence of clinical UGI bleeding than those taking aspirin alone (26).

In summary: 1) Unbuffered aspirin, with and without alcohol, predisposes to upper gastrointestinal bleeding; 2) Alcohol alone may play a role in individuals with altered gastric mucosa; 3) Buffering aspirin will prevent bleeding, even when alcohol is taken at the same time.

Our experience at the DVAH is shown in Table 3.

Table 3.

Drug Use in DVAH Bleeders

Total Patients:	100
No. Using Aspirin :	16
No. Using Alcohol :	50
No. Using Both :	8
No. Using Neither :	26

If a patient presents with an UGI bleed, then, what factors will worsen his prognosis? One almost universally accepted factor of poor prognosis is *age*, there being an almost three-fold increase in mortality for patients over 60 years of age (1,3,33). Another adverse situation, although not as serious as older age, is the presence of *coincidental disease* (32). While it makes sense that bleeding in patients with severe cardiovascular disease would eventuate in more serious outcome, it is also a fact that fully 65% of our patients at the DVAH had another serious, chronic disease.

Certain *specific lesions* are said to lead to a higher mortality with bleeding varices (1,3,33,41), stress gastritis (1,3,32), and gastric ulcer (33,41) frequently mentioned. The first two lesions occur in patients with other illnesses, and gastric ulcer tends to develop in older people, situations which may mask any true significance of the lestions per se.

Clearly, and logically, the *volume and rate of blood loss* is important. Patients who bleed more stand a greater chance of dying. What is not clear is the most accurate means of determining the amount of blood lost. The occurrence of hematemesis is said to indicate a large blood loss, perhaps over 25% of the circulating blood volume, and portend a higher mortality (33,35). This was not the case at the DVAH.

More helpful are those observations which reflect the level of circulating red blood cells and blood volume at the time one sees a patient. Table 4 displays the parameters indicative of either blood loss greater than one liter or an increased mortality (3,37-39).

Table 4.

Response to Blood Loss

Parameter	1 liter Loss	↑Mortality
Anemia	<11 gm%	<8 gm%
Pallor	Yes	---
Tachycardia	>100/min	---
Hypotension	<100 mmHg	<80-100 mmHg

To interpret these parameters too literally, however, will expose one to the cardinal danger in the management of UGI bleeders -- underestimation of severity. To put these values in perspective requires a review of the physiologic compensatory responses following an acute UGI bleed (40).

The hematocrit and blood pressure in a bleeding patient is basically a reflection of three factors: the volume of blood lost; the rate at which it is lost; and the degree of volume replacement. Following the removal of 20% of the circulating blood volume (1000 ml), (Figure 5), there is an immediate fall in blood pressure, a rise in heart rate, and vasoconstriction. The hematocrit, of course, remains unchanged. Only as, first, protein poor and, later, protein rich fluid enters the vascular tree from extravascular compartments does the hematocrit fall and blood pressure rise.

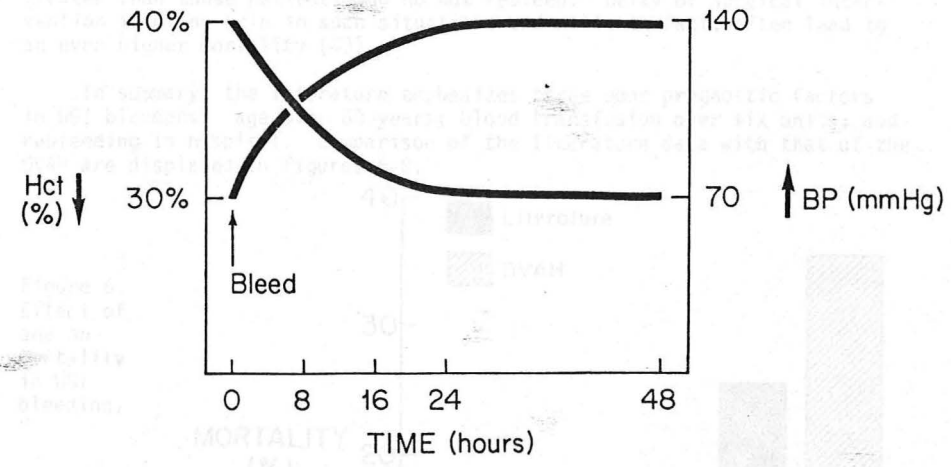

Figure 5. Response of hematocrit and blood pressure after removal of 1000ml blood.

The heart rate may soon return to normal or actually fall below normal and is then an unreliable sign. The level of the hematocrit depends on the rapidity and completeness of vascular reconstitution and, unless low, is of dubious

help. The blood pressure is the most important sign and most accurately mirrors the severity and emergency of the situation. Even so, the patient's age, pre-existing blood pressure, and ability to mobilize fluid can alter this response. Thus, a low hematocrit, low blood pressure, or rapid heart rate are helpful; a normal hematocrit, normal blood pressure, or normal heart rate must be interpreted very carefully in the light of all the extenuating circumstances.

Another, more ultimate, measure of blood loss is the blood transfusion requirement. While these figures obviously reflect bias as to the "acceptable hematocrit", rate of blood loss, and incidence of rebleeding, several studies clearly show that the mortality for patients receiving over six units of blood is 2-8 times higher than those requiring less. The mortality when over ten units of blood are required is some 6-24 times higher (3,32,33). One misguided conclusion from such data is that a patient who requires over six units of blood is automatically a surgical candidate. These patients die because their hemorrhage is more extensive, not because they have had surgery delayed. Indications for surgery depend upon the specific responsible lesion and the risk of surgery in each individual, not just a particular transfusion requirement.

One final ominous prognostic situation is a *recurrence of hemorrhage* in hospital (41,42). Up to 30% of UGI bleeders rebleed in hospital, usually within 48 hours of admission, and most often from varices and gastric ulcer. Some 50% will require surgery with an ultimate mortality that is 4-7 times greater than those patients who do not rebleed. Delay of surgical intervention is of no help in such situations and will, in fact, often lead to an even higher mortality (43).

In summary, the literature emphasizes three poor prognostic factors in UGI bleeders: age over 60 years; blood transfusion over six units; and rebleeding in hospital. Comparison of the literature data with that of the DVAH are displayed in figures 6-8.

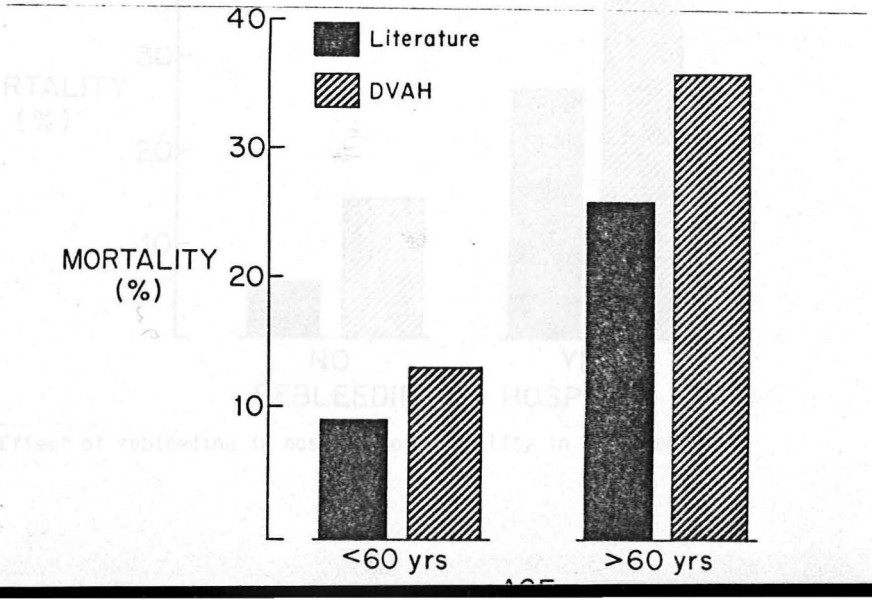

Figure 6. Effect of age on mortality in UGI bleeding.

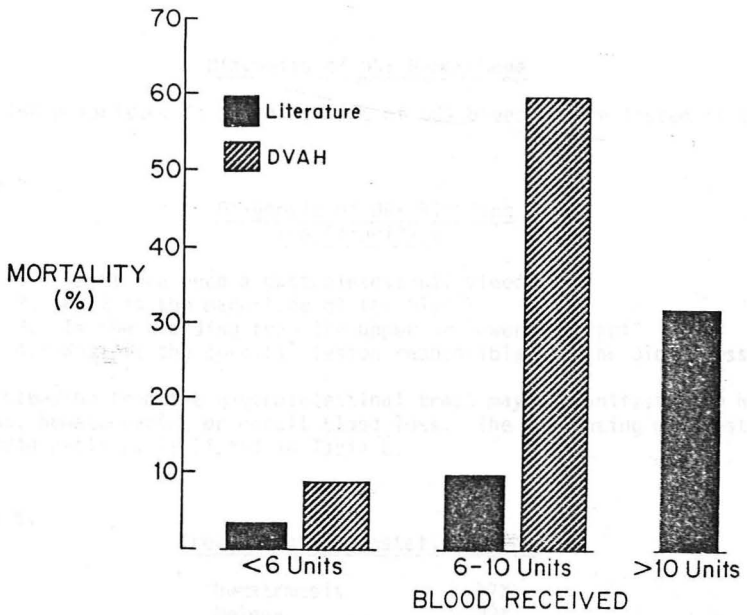

Figure 7. Relation of transfusion requirement and mortality in UGI bleeding.

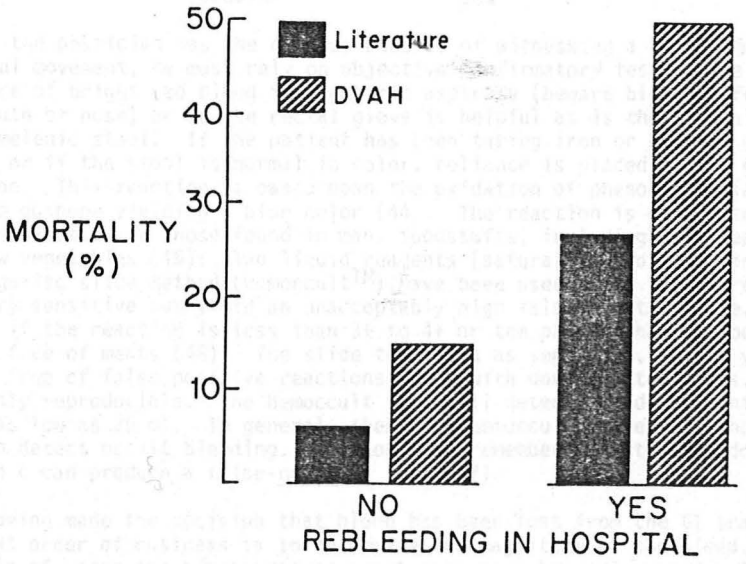

Figure 8. Effect of rebleeding in hospital on mortality in UGI bleeding.

Diagnosis of UGI Hemorrhage

The priorities in the diagnosis of UGI bleeding are listed in Table 5.

Table 5.

Diagnosis of UGI Bleeding
The Priorities

1. Has there been a gastrointestinal bleed?
2. What is the magnitude of the bleed?
3. Is the bleeding from the upper or lower GI tract?
4. What is the specific lesion responsible for the blood loss?

Bleeding from the gastrointestinal tract may be manifested by hematemesis, melena, hematochezia, or occult blood loss. The presenting manifestation in the DVAH patients is listed in Table 6.

Table 6.

Presenting Manifestation (DVAH)

Hematemesis	17%
Melena	32%
Both	26%
Hematochezia	7%
Occult	18%

Unless the physician has the dubious benefit of witnessing a bloody emesis or bowel movement, he must rely on objective confirmatory tests. The presence of bright red blood in a gastric aspirate (beware bleeding from the mouth or nose) or on the rectal glove is helpful as is the typical black, tarry melenic stool. If the patient has been taking iron or bismuth medications, or if the stool is normal in color, reliance is placed on the guaiac reaction. This reaction is based upon the oxidation of phenolic guaiacetic acid to quinone yielding a blue color (44). The reaction is catalyzed by heme peroxidases or those found in many foodstuffs, including dark meats and raw vegetables (45). Two liquid reagents (saturated or dilute tincture) and a guaiac slide method (Hemoccult™) have been used. The liquid reagents are very sensitive but yield an unacceptably high false-positive rate, especially if the reaction is less than 3+ to 4+ or the patient has not been on a diet free of meats (46). The slide test is ¼ as sensitive, but is virtually free of false positive reactions, even with unrestricted diets, and is highly reproducible. The hemoccult test will detect blood loss into the stool as low as 25 ml. In general, then, the hemoccult slide test should be used to detect occult bleeding. It should be remembered that large doses of vitamin C can produce a false-negative test (47).

Having made the decision that blood has been lost from the GI tract, the next order of business is to determine the magnitude of the bleed. The pitfalls of using the hematocrit or heart rate have been discussed. If the

blood pressure is low when the patient is supine, a significant bleed has occurred; a blood pressure that drops more than 10 mm Hg upon sitting (orthostasis) indicates either a lesser bleed or a partially compensated bleed. The manner in which a GI bleed presents itself is also helpful. A positive stool guaiac indicates something over 25 ml of blood loss; melena usually requires at least 500 ml of blood loss, although intestinal transit time certainly plays a role; and UGI bleeding that manifests as hematochezia implies a loss of over 1000 ml (48).

After the extent of bleeding has been determined by a careful examination, a decision must be made if the bleed is from the upper or lower GI tract. Once again, the clinical presentation is helpful (Table 7).

Table 7.

Site of GI Bleeding Relative to Presentation

HEMATEMESIS	→ ABOVE LIGAMENT OF TREITZ
MELENA	→ ABOVE LIGAMENT OF TREITZ
HEMATOCHEZIA	→ USUALLY LOWER GI OR MASSIVE UPPER GI
OCCULT	→ UPPER OR LOWER

If occult bleeding is present, it is mandatory for diagnosis to place a nasogastric tube. While a positive aspirate is diagnostic of an upper GI bleed, a negative aspirate rules out only bleeding from the esophagus and stomach. Although the source of bleeding in this instance is usually lower GI, an actively bleeding post-pyloric lesion may well be present and other signs must be evaluated. Obviously a nasogastric aspirate may be negative if bleeding has ceased. Hematochezia represents either a very rapid, massive UGI bleed or, more likely, a lower tract bleed. Here the nasogastric aspirate and proctoscopy will be of great help.

Other findings in UGI bleeding include hyperactive bowel sounds (48), leukocytosis (48), fever (49), and elevation of the BUN (48). Elevation of the BUN in acute UGI bleeding has been recognized for years (50), but the mechanism has yet to be fully explained. While a rising BUN may be seen in the absence of shock, mere presence of blood in the gut will not cause such (51). It appears to require a combination of blood loss plus blood in the gut (52). Nevertheless, it remains a helpful indication of an UGI bleed and is a useful guide to the continuing activity or cessation of the bleed.

Only after the presence and severity of a GI bleed has been assessed, appropriate resuscitation has begun, and the source is determined to be upper GI should it be attempted to find the specific lesion present. It is almost inherent in the practice of medicine to wish to make a specific diagnosis whenever possible and elaborate steps are often utilized. That such information is helpful in the proper management of UGI bleeders is logical and, indeed, upper GI x-rays, endoscopy, and angiography are liberally used. Whether or not the patient actually derives benefit by these ministrations is open to question. Hellers has shown that when the failure to make a diagnosis is reduced, the mortality is also reduced (53). In his study, however, a number of other factors may also have contributed, including early surgery, admission to intensive care units, and care by one team of physicians. Himal also believes that a diagnosis prior to treatment reduces mortality (3) (Table 8).

Table 8.

Mortality of UGI Bleeders (% of Each Group)

	No.	Diagnosis Made	No Diagnosis Made	Overall
Operated	212	9.5%	32%	17.5%
Not Operated	418	3.3%	21%	9.6%
Total	630	5.4%	24.7%	12.5%

Interpretation of the data discloses that in the 1/3 of the patients in whom surgery was performed, a diagnosis clearly aided survival. Similar results in the non-operated group are harder to understand. Since medical therapy usually varies little from observation, supportive measures, and perhaps antacids, the increased mortality in those not diagnosed perhaps reflects the inability or undesirability to make a diagnosis because of poor initial condition. Thus, the ability to render a specific diagnosis may be helpful in patients requiring a particular form of surgery but may not be of value in other groups. A general statement can be made that a specific diagnosis is necessary if specific therapy is needed, a matter that will be addressed further in this discussion.

Let us assume for the time that a specific diagnosis should be made. The first step is a careful *history and physical examination.* These will rarely be diagnostic but may lend valuable clues. Tables 9 and 10 list pertinent aspects of each.

Table 9.

The History in UGI Bleeding

Finding	Supposed Associated Lesion	DVAH Experience
Retching	Mallory-Weiss	3/7
Heartburn	Esophagitis	2/6
Dyspepsia	Peptic Ulcer	6/26
Medications (ASA)	AGML	10/12
	Gastric Ulcer	7/13
Past Surgery	Recurrent Ulcer	----
Associated Illnesses	Varices	65% of all patients
	AGML	

Clearly in our experience, the history was of little help in any given patient. Niether were the findings specific for any disease.

Table 10.

The Physical Examination in UGI Bleeding

Finding	Supposed Associated Disease
Cutaneous Lesions	Varices (Spider Angiomata); O-W-R Ehlers Danlos; Pseudoxanthoma elasticum; Blue Rubber Bleb Nevus Syndrome
Jaundice	Varices; hemobilia
Adenopathy	Tumor
Hepatosplenomegaly	Varices
Abdominal Masses	Tumor
Rectal Examination	Tumor

Prior to the advent of fiberoptic endoscopy the standard diagnostic procedure was a barium *upper GI x-ray*. Accuracy was believed to be very good but after endoscopy became readily available it was demonstrated that this radiological technique failed to diagnose most mucosal lesions. Additionally, x-rays may miss varices in over 50% of cases (54) and even if varices are seen, the actual bleeding may be from another lesion (13). Upper GI x-rays are most helpful in the diagnosis of gastric or duodenal ulcer, but even these lesions may be missed, especially in an acutely bleeding patient with clots to obscure the lesions (55). Finally, performance of an upper GI x-ray will leave a residue of barium which may hinder subsequent endoscopy. Obviously the dependability of upper GI x-rays varies with the expertise of the radiologist, and the newer double contrast techniques may be more accurate than standard techniques (56). Nevertheless, barium x-rays are now reserved primarily for the evaluation of chronic blood loss or for the acute bleeder who is not endoscoped early. *Endoscopy*, then, has assumed the major diagnostic role in determining a specific bleeding site and a thorough review of this topic is warranted.

In 1952, Palmer initiated a new era in the management of upper gastrointestinal hemorrhage by advocating a "vigorous diagnostic approach" utilizing esophagoscopy and gastroscopy in addition to traditional radiography (57).

Other authors quickly echoed this philosophy, citing diagnostic "success" rates up to 90% (58-62). Reasons for an increase in accuracy over radiographic techniques alone are cited in Table 11.

Table 11.

Benefits of Endoscopy

1. Determination of mucosal bleeding sites (eg.,Mallory-Weiss lesions, esophagitis, and gastritis) not amenable to radiographic diagnosis (63-65).

2. Discovery of esophageal and gastric lesions missed by x-ray (eg., varices, tumors, ulcers).

3. Correction of radiological false positives.

4. Determination of the actual site of bleeding when x-ray discloses only potential sites of bleeding.

The role of radiology, then, became limited to the detection of duodenal lesions beyond the reach of gastroscopes.

In 1969 Palmer summarized the results in 1400 patients with upper gastrointestinal hemorrhage (67). Using endoscopy and radiography, he was able to correctly diagnose the bleeding site in 93% of the patients. A superficial mucosal bleeding site was responsible in 25% of cases and half of all bleeding patients had other potential sites of bleeding. As with earlier studies, however, the mortality rate of patients was 8%, unchanged from the pre-endoscopy era. A study published two years later confirmed this mortality rate (68). An accompanying editorial admitted that endoscopy offered a greater chance of diagnosis but queried "Does early diagnosis really matter? Does it lessen mortality or recurrence rates? Does it reduce length of hospital stay? Does it prevent unnecessary surgery?" (69). These questions have yet to be answered.

With the advent of flexible fibreoptic endoscopes capable of examining the duodenal bulb and beyond (panendoscopes), the approach to upper gastrointestinal hemorrhage became even more endoscopically oriented (70). Recent reviews list early endoscopy as the prime tool in diagnosis of upper gastrointestinal hemorrhage in general (71,72); upper gastrointestinal hemorrhage in cirrhotics (13,73,74); and hemorrhage in patients with cancer (75,76). Indeed, a recent interview in Hospital Tribune, a widely distributed medical newspaper, labeled gastroscopy "a 'must' for patients vomiting blood." (77)

Cases #3-4-5

G.B., a 52 year old man who admitted to drinking one fifth of gin per day for six years, presented to the DVAH after vomiting blood and passing a melenic stool. Blood pressure was 100/80 supine falling to 85/60 on sitting. Nasogastric aspirate was positive for blood, the bowel sounds were hyperactive,

and stool was black, guaiac positive. After stabilization with intravenous fluids and two units of blood, he underwent upper GI x-rays and endoscopy.

Case #6

B.L. was a 24 year old man in excellent health prior to eating some "bad beans". He vomited the offending beans followed by two clear emeses and then a bloody emesis. Blood pressure on arrival at the DVAH was 120/80 with no postural changes and nasogastric aspirate was positive. Upper GI series was performed followed by endoscopy.

Cases #7-8-9

P.T., a 72 year old man, presented to the DVAH after having fainted while mowing his lawn. He told of taking eight aspirin per day for the previous month because of headaches. On arrival his blood pressure was 80/60 and his heart rate 80. After beginning fluids, his physician passed a nasogastric tube, aspiration of which revealed bright red blood. This cleared with lavage. Following resuscitation he had an UGI series and endoscopy.

Case #10

Z.B. was a 62 year old man who told of a 30-pound weight loss, early satiety, and post prandial epigastric pain. On arrival to the DVAH his blood pressure was 160/95 but he appeared pale. A hematocrit was 18% and stool guaiac was 4+ positive. He underwent an UGI series and endoscopy.

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The bulk of the literature comparing the diagnostic accuracy of endoscopy vs UGI series are "experience" accounts. In reviewing eleven such series from 1973 to 1974, one finds data as depicted in Table 12 (78-85, 88-90).

Table 12.

Accuracy of Endoscopy vs UGI Series

Procedure	No.	True Pos.	False Pos.	False Neg.
Endoscopy	1200	82% (53-96%)	2% (0-9%)	6% (0-26%)
UGI Series	800	41% (30-84%)	6% (2-11%)	44% (13-67%)

While radiological techniques give a relatively low rate of false positive diagnoses, most of these studies do show that early panendoscopy is far more accurate in determining the cause of an upper gastrointestinal hemorrhage. Careful analysis of these data, however, discloses a number of important points:

1. All of these are poorly controlled, non-randomized studies.

2. There is a very wide range of results in the accuracy of these techniques. Possible explanations for this disparity include the following:

   a. The definition of a "bleeding site" and the standards by which a final diagnosis is rendered varies from study to study. In two studies where active bleeding or a clot is required at endoscopy to define a bleeding site, endoscopy provided a true positive result in only 53% and 65% of the cases (82,90). In a study by Fraser in which surgical confirmation was required as the standard for a final diagnosis, barium meal yielded a true positive diagnosis in 84% of the cases, far greater than the average result (90). Does this imply that radiological techniques are as adequate as endoscopy when only bleeding lesions requiring surgical intervention are evaluated?

   b. The timing of endoscopy is important. If endoscopy is delayed beyond forty-eight hours, there is a far greater chance of finding no lesion (79,82). If bleeding lesions can be so evanescent, of what value is it to discover them early on?

   c. Experience in performing endoscopy and doing high quality barium meal studies must be quite variable.

   d. In the series with a higher incidence of superficial mucosal lesions, UGI series expectedly fares less well than endoscopy.

   e. The need for surgical intervention varies from 10-40% of the patients, indicating differences in either etiology or severity of bleeding.

3. Using all diagnostic modalities available, no diagnosis was ever made in an average of 17% of bleeders (0-43%). A study comparing the experience during the flexirigid gastroscope era (1962) with the flexible panendoscope era (1972) confirms a greater detection of mucosal lesions but shows no change in the incidence of undiagnosed cases (18 vs 22%) (84).

4. Mortality from an upper gastrointestinal bleed ranges from 4-15%, with an average of 8%. This figure is confirmed by other studies (62,67,68,91,92,97) and is no less than in the "pre-endoscopy" era.

5. Of 1286 patients examined, only two of the 19 with gastric carcinoma had the lesion missed by UGI series.

In summary, early panendoscopy may well disclose more lesions, especially mucosal lesions, than UGI series in patients with acute upper gastrointestinal bleeding. A number of poorly controlled studies involving widely disparate patient groups have failed, however, to delineate any significant benefit to the patient, any reduction in undiagnosed bleeding episodes, or any improvement in survival (85, 87).

Recently, randomized studies by Sandlow et al and Allan Dykes have disclosed greater diagnostic accuracy for endoscopy (93,94). Sandlow's study however, really compares early endoscopy and/or UGI series. Using this combined early approach they found no benefit regarding duration of hospital stay, rebleeding, need for surgery, morbidity or mortality (8% again) with the aggressive approach (93). The only diagnostic errors, in fact, occurred in two aggressively managed patients. Dykes and Allan compared routine early endoscopy and UGI series versus these procedures done only for selected patients. They conclude that "the use of routine endoscopy adds information to a substantial number of patients with gastrointestinal bleeding sufficient to alter management and probably to improve prognosis" (94). No data is presented to support these contentions and, indeed, mortality was 8% in either group.

Two "controlled," randomized, prospective studies have been published comparing early endoscopy versus early UGI series in upper gastrointestinal bleeding (95,96). These studies deserve detailed analysis. Morris et al randomly assigned sixty patients with mild to moderate upper gastrointestinal bleeding to either endoscopy or UGI series as the initial study. If no diagnosis was made on the initial study, the other study was performed. There was, however, no true control group, for 46 of the 60 patients ultimately underwent endoscopy. Of these 46 patients, 34 had a definite diagnosis made (74%) compared with 8 of 37 diagnosed by barium meal (21%). Three patients had no definite diagnosis made after one study and another 15 were unable to be diagnosed after both studies (30%). As expected, UGI series failed to diagnose mucosal lesions, the final diagnosis in almost 40% of their cases. Interestingly, all five deaths (8%) occurred in the group initially randomized to endoscopy. Once again, then, early endoscopy has not been shown to alter mortality or benefit the patient in a definable fashion.

The most recent study by Keller and Logan attempts to show that emergent endoscopy does indeed statistically benefit patient management. Sixty-eight patients with an upper gastrointestinal hemorrhage requiring either three or more units of blood transfusion or surgery within 24 hours of admission were randomized. Patients received either emergent endoscopy followed by UGI series or vice-versa. Once again, no true control group is present. Table 13 displays the results in terms of diagnostic accuracy.

Table 13.

Diagnostic Accuracy of Endoscopy and X-ray

	Endoscopy			X-ray		
	First Procedure	Second Procedure	Both Procedures	First Procedure	Second Procedure	Both Procedures
Correct	23(74%)	23(79%)	46(72%)	10(36%)	8(32%)	18(34%)
Incorrect	12(26%)	6(21%)	18(28%)	18(64%)	17(68%)	35(66%)
	35	29	64	28	25	53

From Keller and Logan. Gut 17:180, 1976.

Endoscopy, whether performed first or second, clearly is more accurate in making a diagnosis. As expected, UGI series failed to diagnose superficial mucosal lesions.

While there was no difference in mortality between the two groups, the patient management was felt to be changed in a favorable fashion following endoscopic diagnosis of the bleeding lesion while incorrect diagnoses resulting from UGI series "adversely" affected patient management. Two points deserve mention. First, optimal management consisted of only three possibilities: surgery; the use of a Sengstaken-Blakemore tube; or neutralization of gastric contents. If one dismisses the 15 patients requiring surgery, one finds only four patients needing a Blakemore tube, while the remaining 49 all require the same treatment - acid neutralization. It is likely that a Blakemore tube would be used only if a patient continued bleeding. Thus, if one considers patients who neither need surgery nor continue bleeding, all are treated alike. What difference can it make to diagnose the bleeding site? Second, even though 18 incorrect diagnoses were rendered by endoscopy, this knowledge resulted in only three changes from correct to incorrect patient management. These data suggest that unless a patient continues to bleed and/or requires surgery, endoscopic delineation of the bleeding lesion is not beneficial to the patient.

Thus, early panendoscopy reliably discloses the lesion responsible for upper gastrointestinal hemorrhage and has become the diagnostic procedure of choice at many centers in this country. That this approach significantly alters a given patient's prognosis has yet to proven adequately. Only if endoscopy will dictate specific therapy for a patient does it seem truly indicated.

Reassuring in one respect is the low morbidity and mortality associated with endoscopy. A recent survey (Table 14) discovered a complication rate of 1.32 per 1,000 procedures and a mortality of less than 1 per 1,000.

Table 14

COMPLICATIONS OF ENDOSCOPY

NO. STUDIES	→	211,410
MORBIDITY	→	507
MORTALITY	→	13 (5 perforation; 2 bleeding; 6 cardiopulmonary)

FROM MANDELSTAM et.al. GASTRO. END. 23:16,1976.

Based on the foregoing data, the following conclusions may be made:

1. A diagnosis must be made any time the specific lesion found will dictate a specific therapeutic intervention.

2. Specific therapy is indicated in any patient continuing to bleed despite gastric lavage; any patient who rebleeds in hospital; and any patient in whom surgery is contemplated.

3. There is as yet no conclusive evidence that failure to make a specific diagnosis in any other situation will adversely affect the patient.

4. In light of the ease and safety of early endoscopy, and until controlled studies dictate otherwise, this procedure will remain the initial procedure in patients with UGI hemorrhage.

The endoscopic experience at the Dallas VA Hospital has been evaluated with a retrospective review of the records of all patients discharged with a diagnosis of UGI hemorrhage for 1975. Twenty-two of the 100 patients were not endoscoped for a variety of reasons (myocardial infarction, patient refusal, believed "unnecessary", bleeding too brisk). Of the 78 patients endoscoped, the procedure was deemed incomplete in 11 because of technical difficulties or the presence of retained gastric debris (food or blood). Even in these cases, either a definite or probable diagnosis was made or the bleeding area noted in 9 patients. Table 15 displays the final diagnoses and the endoscopic contribution to these diagnoses in 100 patients.

Table 15.

Diagnosis of UGI Hemorrhage (DVAH)

		Endoscopy			
	No.	Definite or Probable Diagnosis	Site Seen	No Diagnosis	Not Performed
Esophagitis	6	6			
Varices	10	7		2	1
Mallory-Weiss	7	6	1		
AGML	12	8			4
Gastric Ulcer	13	11		1	1
Duodenal Ulcer	13	10		1	2
Cancer	4	1	2		1
Other	2	2			
	67	51	3	4	9
No Diagnosis	33		7	13	13
	100	51 (65%)	10 (13%)	17 (22%)	22

Of the 78 patients endoscoped, a definite or probable diagnosis was made in 51(68%); the bleeding site was seen in another 10 (13%); and no diagnosis was rendered in 17 (22%). While the inability to make a diagnosis is somewhat higher than figures cited in the literature, this may be a reflection of endoscopic honesty rather than less competent endoscopists. Table 16 lists the means of diagnosis in the 16 patients in whom endoscopy could not make either a definite or probable diagnosis.

Table 16.

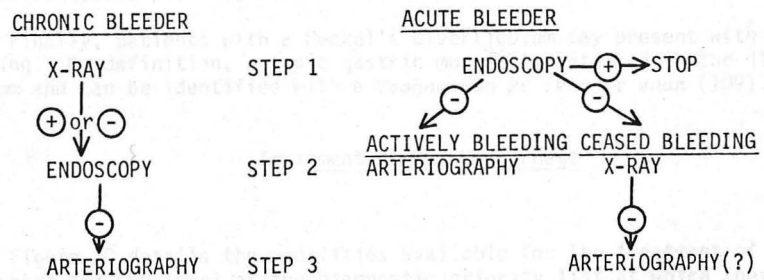
Means of Diagnosis
When Endoscopy Fails

Total No.	16
UGI	5
Surgery	4
Autopsy	2
"Best Guess"	5

In contrast to some reports in the literature, the mortality in patients with no diagnosis at the DVAH was no greater than the mortality in patients with a diagnosis.

Although endoscopy has supplanted the UGI X-ray as the procedure of choice for upper gastrointestinal bleeding, another radiological procedure, *arteriography*, plays an important role (99-107). The use of arteriography takes three forms: diagnosis in an acutely bleeding patient when endoscopy is negative or cannot be performed; diagnosis in the chronic bleeder when endoscopy and conventional UGI series are negative; and in the treatment of bleeding when less invasive measures fail. Figure 9 outlines the sequence to be taken in the diagnosis of acute and chronic UGI bleeding.

Figure 9. Diagnostic sequence in UGI bleeding.



Detection of an active arterial bleeding site requires a blood loss of 0.5-0.6 ml. per minute (101). If such is the case, a catheter is threaded up the aorta via the femoral artery. If an aorta-enteric fistula is suspected, a midstream aortogram is first performed. Otherwise, the angiographer proceeds directly with selective celiac axis arteriography. If a lesion is not detected, the arteriographer carries out selective left gastric, gastroduodenal, splenic, and superior mesenteric artery injections. If there is active arterial bleeding at the time of arteriography, the procedure will almost invariably disclose it. Esophageal and gastric lesions bleed primarily from the left gastric artery while duodenal lesions arise from the gastroduodenal artery. If no extravasation of contrast material is seen, the nasogastric aspirate remains positive, and prior endoscopy has disclosed the presence of varices, it can be assumed that a ruptured varix is the source of hemorrhage. Only rarely will extravasation of venous blood be noted. Following determination of the bleeding site, the catheter can be positioned in the appropriate artery and employed for infusion of vasoconstrictor drugs in an attempt to arrest the bleeding. (See Treatment of UGI Hemorrhage)

A second use of arteriography is as an elective procedure in the non-bleeding patient. Situations where it may benefit include the acute bleeder who has ceased bleeding or the chronic bleeder in whom endoscopy and UGI X-rays have failed to delineate the lesion (Figure 9). In such cases, angiography will succeed in locating a lesion in about 50% of the cases (107). Lesions to be sought include arterio-venous malformations (especially of the ileocecal area); tumors; and aneurysms.

Occasionally there are patients in whom barium x-rays, upper endoscopy, and arteriography are all negative but who continue to bleed slowly. If an unrewarding evaluation for a colonic bleeding site has also been carried out, it is assumed that these patients are bleeding from the small intestine somewhere between the ligament of Treitz and the ileocecal valve. Until extremely long endoscopes become available, reliance must be placed on either the fluorescein string test of a *long intestinal tube*(108). With this latter technique, a slender plastic tube is passed through the mouth into the small intestines. A finger cot filled with mercury is attached at the leading edge to form a traction bolus. As the tube advances into the small bowel periodic samples of intestinal juice are removed by a syringe and tested by the guaiac method. When the level of bleeding is reached and guaiac becomes positive, the length of tubing inserted is noted and a selective small bowel barium x-ray is performed. This procedure, of course, requires enough continued bleeding to produce guaiac positive stools.

Finally, patients with a Meckel's diverticulum may present with UGI bleeding. By definition, ectopic gastric mucosa is situated in the diverticulum and can be identified with a *Technetium 99 isotope scan* (109).

Treatment of UGI Hemorrhage

Figure 10 details the modalities available for the treatment of UGI hemorrhage and the level of the diagnostic priority list at which they are employed. Just as the diagnostic sequence begins with basic measures,

treatment must also start with a basic, general approach.

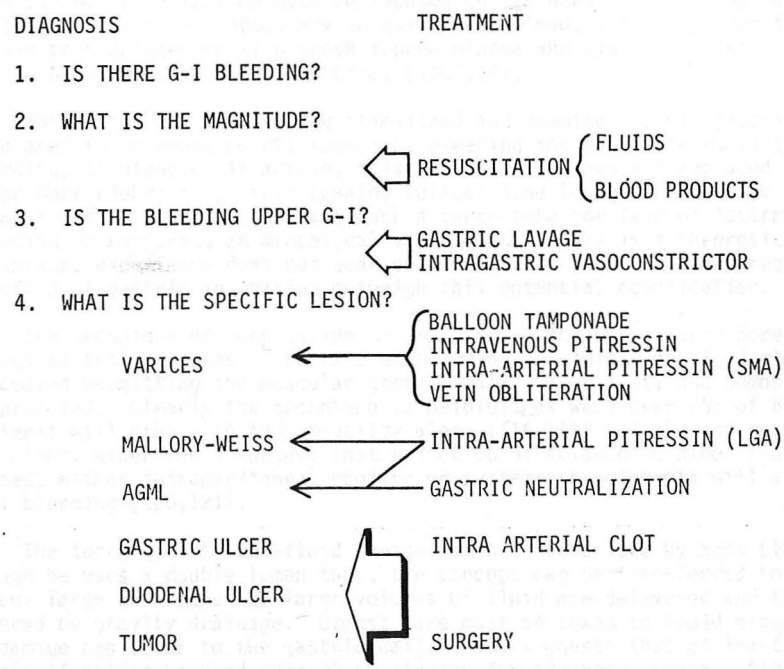


Figure 10. Diagnosis and treatment of UGI hemorrhage.

As soon as it is evident that a patient has bled, especially if massively, resuscitative measures are begun. *Resuscitation* is geared toward supporting the vascular volume and providing adequate tissue oxygenation. Notwithstanding rare studies minimizing the need or safety for volume expansion (112), large intravenous catheters, perhaps into the subclavian vein, must be inserted and fluids begun. Urine output and, if necessary, pulmonary wedge or central venous pressure are monitored as is the systemic blood pressure. Blood is sent for laboratory data, typing, and cross matching. Particulary important are determinations of clotting factors. Oxygen may be necessary.

Blood is transfused depending upon the patient's clinical state and, to a degree, on the early hematocrit. Remember the shortcomings of the hematocrit interpreted by itself. Once blood is begun, the end point is determined

not by following the hematocrit alone, but combining this data with the rate of continuing bleeding and the patient's overall clinical status. The practice of under-transfusion to minimize continued bleeding has been shown to have no basis in fact (113). In patients who receive large transfusions or in patients with cirrhosis, attention must be focused on the need for clotting factors and platelets. It is not necessary to give fresh blood, but every four to six units should be supplemented with fresh frozen plasma and platelet packs. Vitamin K should be administered to cirrhotics (110,114).

While the patient is being stabilized and examined, a nasogastric tube is placed to document an UGI source of bleeding and gauge the rapidity of bleeding. If bleeding is active, this tube is withdrawn and replaced with a large bore (36Fr) orogastric (Ewald; Edlich) tube for gastric lavage. There is at times a reluctance to pass such a large tube for fear of "stirring up", bleeding or rupturing an esophageal varix. While this is a theoretical disadvantage, experience does not bear out such fears (115). In any regard, the benefits of gastric intubation outweigh this potential complication.

The technique of iced-saline *gastric lavage* through a large bore tube serves several purposes. The rate of bleeding is indicated; blood clots are evacuated permitting the muscular gastric wall to contract; and hemostasis may be promoted. Clearly the technique is helpful, as well over 75% of bleeding patients will stop with this modality alone (116-119). While the mechanism is not clear, experiments suggest that reduction of splanchnic blood flow occurs. Indeed, either intraperitoneal cooling or systemic hypothermia will also control bleeding (120,121).

The technique of iced-fluid lavage has been described by Moss (122). Although he uses a double lumen tube, the concept can be transferred to a single lumen, large bore tube-ie, large volumes of fluid are delivered and then recovered by gravity drainage. Utmost care must be taken to avoid excess suction, as damage can occur to the gastric wall. Moss suggests that at least 10 liters of saline be used over 30-60 minutes for adequate lavage. Although iced saline is the usual fluid, evidence is available that iced water is as effective and safe (123).

Wangansteen has popularized an elaboration of gastric lavage-ie., gastric cooling by a continuously perfused gastric balloon (124). Other investigators have confirmed the efficacy of this technique (125-127) but little seems to be gained over simple manual lavage.

If gastric lavage and cooling fails to arrest bleeding, one other general therapeutic modality has been proposed. Beginning with that of LeVeen in 1972, four studies have reported the efficacy of vasoconstrictors (Levophed) either intragastrically or intraperitoneally (128-131). While these studies are all uncontrolled, they report a high degree of success (55-90%) in slowing bleeding with no complications. As a "stop-gap" measure, then, the instillation of 8 mg Levophed in 100 ml of normal saline may be tried. Caution must be exercised, however, not to rely on this form of therapy to the exclusion of other proven and more specific modalities.

With vigorous gastric lavage and, perhaps, intragastric vasoconstrictors, most UGI bleeders will cease bleeding. If not, more definitive therapy is needed and of necessity demands a specific diagnosis be made, either by endoscopy or arteriography. Because any individual patient, be he cirrhotic or not, can bleed from any lesion, a specific diagnosis must precede specific therapy.

Esophageal Varices

Bleeding esophageal varices present a most difficult problem. The standard form of therapy until the late 1960's was *balloon tamponade*. Although this concept was originated in 1930, it was 1950 when Sengstaken and Blakemore devised the standard double balloon device (134). With few exceptions, this design has been used since (Figure 11). The proper techniques for this device should be reviewed prior to each use.

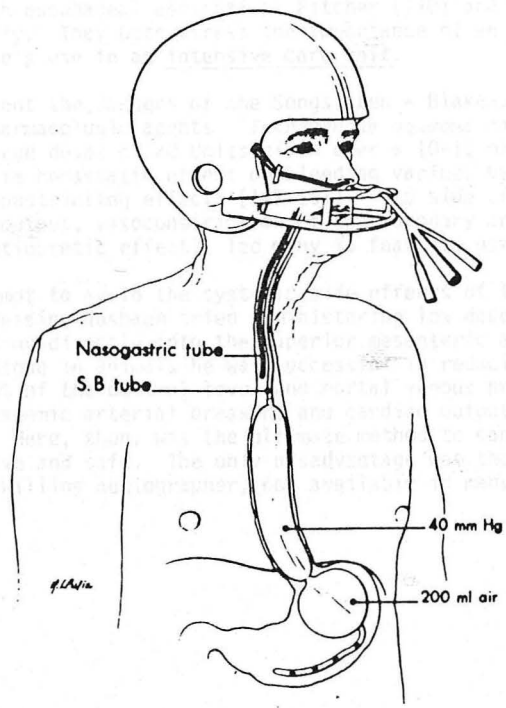


Figure 11. The Sengstaken - Blakemore tube.

Liedberg in reviewing the experience with the Sengstaken - Blakemore tube concluded that the technique was effective in the temporary control of bleeding from esophageal varices but rebleeding was frequent and the ultimate prognosis was grave. Emphasis was placed on the complications of its use:

Esophageal rupture or erosion
Asphyxia from occlusion of the airway
Pulmonary aspiration

Conn and Orloff warned that the use of this tube has close to a 40% morbidity rate and a 20% mortality rate (136-138). Since then, a number of studies have paid close attention to the prevention of these complications with a reduction in mortality to 2-6% (139-143). Although morbidity remains relatively high, the cessation of bleeding is effected in almost 90% of the cases. The most important modification of the Sengstaken - Blakemore tube is the addition or placement of an aspiration tube above the esophageal balloon as first proposed by Linton (144) and popularized by Edlich (145) and Pitcher (140). Linton's original tube, however, has only one balloon (gastric) and is felt by some to afford inadequate tamponade with excessive complications (143). Using the two-balloon tube with esophageal aspiration, Pitcher (140) and Bauer (142) report very low mortality. They both stress the importance of an experienced team managing the tube's use in an intensive care unit.

To circumvent the dangers of the Sengstaken - Blakemore tube, attention was turned to pharmacologic agents. *Intravenous aqueous vasopressin* (Pitressin) in relatively large doses of 20 Units given over a 10-15 minute period was found to have a definite hemostatic effect on bleeding varices by virtue of its splanchnic vasoconstricting effects (147-151). Its side effects, however (decreased cardiac output, vasoconstriction of the coronary arteries, tachyphylaxis, and an antiduretic effect), led many to fear its use (152, 153).

In an attempt to avoid the systemic side effects of large dose, intravenous vasopressin, Nusbaum tried administering low dose, constant infusions of the drug directly into the superior mesenteric artery (154). Using this technique in animals he was successful in reducing splanchnic blood flow to 60% of the control level and portal venous pressure to 50% (Figure 12). Systemic arterial pressure and cardiac output were said not to be affected. Here, then, was the ultimate method to control bleeding varices, effective and safe. The only disadvantage was the need for an experienced and willing angiographer, not available in many hospitals.

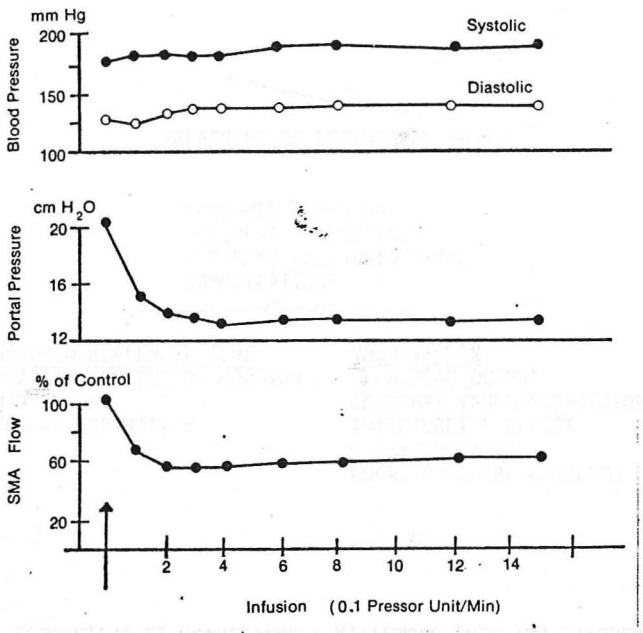


Figure 12. Effects of superior mesenteric artery infusion of vasopressin.

This technique of *intra-arterial vasopressin* was then applied with success to humans (155), and between 1968 and 1973, their group treated 41 patients (156). Using 0.1 to 0.4 Units per minute, they were able to arrest bleeding from esophageal varices in 40 patients. Two of the 18 patients who were able to undergo shunt surgery ultimately died as did all 23 of those who did not have surgery. Several local arterial complications (bleeding, thrombosis) were noted but with the exception of bradycardia, no cardiac side effects occurred. Some authors have since reported up to an 80% success rate (157), while others note slightly lower success rates with a very high rate of recurrence (158,159). Vascular complications have been stressed (160). Figure 13, then, compares the effects of vasopressin administration for the control of variceal bleeding with the Sengstaken - Blakemore tube.

TREATMENT OF ESOPHAGEAL VARICES

CONTROLS BLEEDING
FREQUENT REBLEEDING
ULTIMATE PROGNOSIS GRAVE
COMPLICATIONS

SENGSTAKEN-BLAKEMORE TUBE	VASOPRESSIN
ESOPHAGEAL RUPTURE OR EROSION	↓CARDIAC OUTPUT
ASPHYXIA	CORONARY VASOCONSTRICTION
PULMONARY ASPIRATION	ANTIDIURETIC EFFECT
	TACHYPHYLLAXIS
	LOCAL ARTERIAL PROBLEMS

Figure 13. Comparison of Sengstaken - Blakemore tube and vasopressin for variceal bleeding.

In 1972 Conn reported similar success in stopping variceal bleeding but was alarmed at a rather high rate of complications, including cardio-respiratory arrest, bacteremia, and intestinal necrosis (161). To evaluate this new technique, he undertook the only randomized, controlled study yet published (162). Although documentation of the bleeding site was less stringent than we would now demand, 33 patients were felt to be bleeding from varices. Four of sixteen randomized to conventional therapy alone ceased bleeding for 24 hours, compared to 12 of 17 randomized to conventional therapy plus superior mesenteric artery vasopressin. Rebleeding was frequent in both groups and the ultimate survival was the same, only 50%. Conn compared this poor prognosis, even when bleeding was controlled, to that of prophylactic portal caval shunts. Patients who had such shunts bled less frequently but had no increase in ultimate survival.

Criticisms of Conn's study include not using balloon tamponade, another effective means of controlling bleeding, as part of conventional therapy, and giving vasopressin to the 12 patients who did not respond to conventional therapy. The fact that 7 of these patients so treated survived and were included in the control group may have masked a favorable effect of vasopressin.

Although a number of complications occurred with vasopressin (bradycardia, other arrhythmias, cardiac arrest, and peripheral embolism), most were trivial and none were lethal. There was no bacteremia or intestinal necrosis. In summary:

1. Both balloon tamponade and selective intra-arterial vasoconstriction effectively arrest bleeding from esophageal varices.

2. Both procedures are fraught with side-effects. Which procedure is elected depends upon the facility and safety with which they may be carried out in any given hospital setting.

3. Both measures must be regarded as "stop-gap" with ultimate survival dependent on other factors.

4. Further controlled studies are essential to delineate the proper role of each modality in variceal bleeding.

Doubt has been further cast on the freedom from cardiac changes and even the mechanism of action of low dose intra-arterial vasopressin. Madden has shown in dogs (163) and Millette in man (164) that intra-arterial vasopressin does result in a significant reduction in cardiac output. Millette has additionally demonstrated only a rather slight decrease in portal vein pressure following the superior mesenteric artery infusion of vasopressin. He concludes that "if selective infusions of vasopressin into the superior mesenteric artery is efficacious in the control of bleeding varices, the therapeutic effect cannot be totally explained by the lowering of the portal venous pressure..." Of tremendous interest, then, is new work by Barr (165) in which a constant, low-dose infusion of vasopressin intravenously produces marked reduction in mesenteric blood flow and portal pressure,with a reduction in cardiac output no greater than that seen with intra-arterial vasopressin. Furthermore, Sirinek (166) has shown that the addition of isoproterenol to this regime prevents any decline in cardiac output while still allowing the portal vein pressure to fall. Using this technique, Athanasoulis has successfully and safely treated 10 patients with bleeding varices (106). Only time and controlled experiments will tell whether this newest variation on a theme has long standing merit. Certainly the ease of administration and freedom from intestinal ischemia is attractive.

Yet another, very new and yet experimental, approach to bleeding varices involves *direct occlusion of the left gastric vein* feeding the varices. Lunderquist in 1974 (167) described a technique of percutaneous transhepatic portal venipuncture followed by manipulation of a plastic catheter into the left gastric vein and subsequent sclerosis of the vein with hypertonic glucose. Four of four patients so treated had successful obliteration. A transjugular approach to the same vessel (jugular vein►vena cava►hepatic vein►portal vein►left gastric vein) has been performed in dogs (168) and now in man (169). In the latter case (Figure 14), bleeding which had not been controlled by intra-arterial vasopressin, a Sengstaken - Blakemore tube, or an emergency mesocaval shunt, was arrested after embolization of Gelfoam particles.

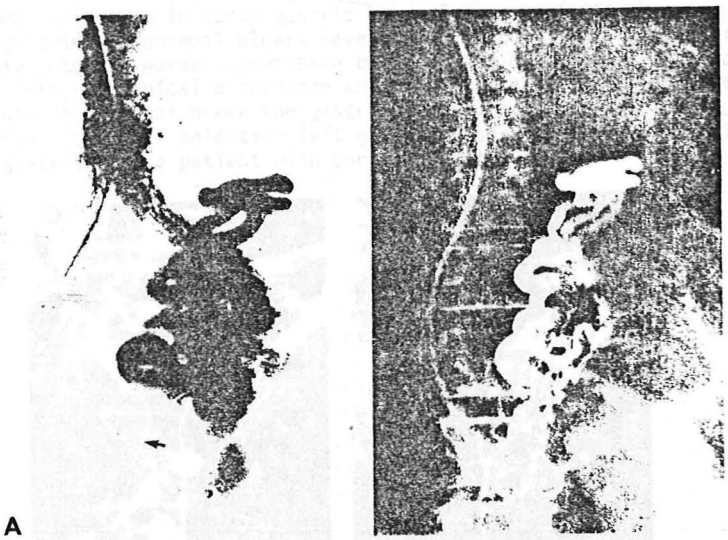


Figure 14. A. Pre-embolization venogram demonstrates a large chain of esophageal and gastric varices. B. Post embolization venogram shows obliteration of the esophageal varices with patency of the gastric varices. From Goldman M. Radiology 118:453, 1976.

Thus, the poor results of surgical therapy and the desperate clinical setting of bleeding varices have spawned a number of promising, but incompletely realized,attempts at medical management. Which, if any, will stand the test of time remains to be seen.

Mallory-Weiss and Acute Gastric Mucosal Lesions

Success with intra-mesenteric vasopressin in the control of bleeding esophageal varices led to its trial for arterial bleeding in 1969 (100). Since then, several groups have evaluated this form of therapy (102-104,157,161,162, 172-176). It was quickly realized that good results demanded selective catheterization of the left gastric artery, if at all possible. Two vasoconstrictor agents have been tried - vasopressin and epinephrine. Epinphrine is a very potent agent (177) but its use is complicated by post-infusion vascular dilatation. Used in short bursts over 30-45 minutes, epinephrine stopped bleeding

from Mallory-Weiss tears in 2 of 2 cases reported (174). The drug is about 65% effective in controlling bleeding from acute gastric mucosal lesions (174, 176), but is currently employed (as a celiac artery infusion) only if the left gastric artery cannot be catheterized (176). Vasopressin is almost 100% effective in controlling hemorrhage from a Mallory-Weiss lesion (103, 172, 175) and over 80% effective in acute gastric mucosal lesions (175), but results in bleeding gastric or duodenal ulcers have been disappointing. Fear that vasopressin may actually worsen hemorrhage by producing mucosal necrosis has been dispelled both by clinical experience and experimental data showing that vasopressin infusions do not break the gastric mucosal barrier (178). Figure 15 demonstrates the use of selective left gastric vasopressin in controlling bleeding gastritis in a patient with portal hypertension.

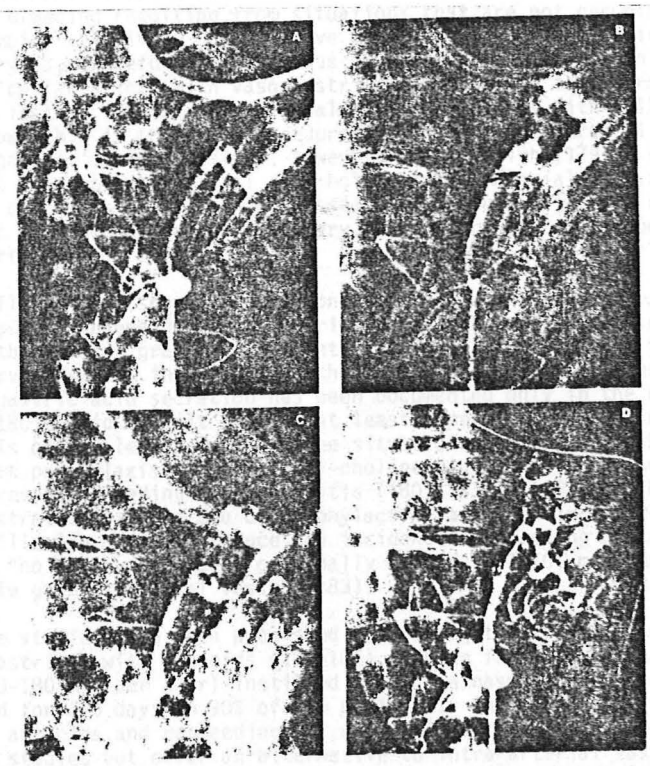


Figure 15. Bleeding gastritis in a patient with portal hypertension. A. Selective left gastric arteriogram, early phase. B. Selective left gastric arteriogram, late capillary phase. There is intense opacification of the mucosa in the body of the stomach with extravasation and accumulation of contrast material in the fundus (arrow). C. The same injection clearly demonstrates ascending esophageal varices. D. Left gastric arteriogram during the infusion of vasopressin shows peripheral vasoconstriction with no extravasation. The infusion was continued for 48 hours, and the bleeding was controlled. From Baum S. Gastrointestinal hemorrhage. Part II: Angiographic diagnosis and control. Adv Surg 7:149, 1973.

The only randomized, controlled study of selective intra-arterial vasoconstrictors has been performed by Conn (162). Five of sixteen patients treated with conventional therapy alone stopped bleeding compared with 8 of 11 also receiving vasopressin. Even more may have responded in the vasopressin group if the perfusion had been carried out each time in the left gastric artery rather than just in the celiac axis. Complications were as reported with the variceal bleeders in the same study and mortality was again unchanged.

The Mallory-Weiss mucosal tear and the acute gastric mucosal lesion are sources of bleeding resulting from situations that are not chronic in nature. To first employ relatively non-invasive means to halt such bleeding rather than surgery is, therefore, meritorious. Occasionally, perfusion of the left gastric or celiac artery with vasoconstrictors will fail to control bleeding from these lesions. Since the surgical risk in patients with Mallory-Weiss tears is low, this is the next procedure of choice. The surgical mortality for acute gastric mucosal lesions, however, is very high (179). In these patients it may prove beneficial to embolize solid material such as autologous clot into the offending vessel, a procedure primarily reserved for gastric and duodenal ulcer. Surgery, in most cases, should be a last-ditch effort.

Finally, a word should be mentioned concerning the use of *gastric neutralization* in bleeding acute gastric mucosal lesions. This lesion occurs in three major groups of patients: those taking aspirin; those with central nervous system injuries; and those undergoing severe stress. While increased gastric acid secretion has been documented only in the neurological patients (180), acid is felt to play at least a permissive role in the pathogenesis of the lesion in all three situations (181). Watts has demonstrated that prophylaxis with an anti-cholinergic drug in neurosurgical patients prevents bleeding from gastritis (180); Silen (181) and Mead (182) have demonstrated that the use of prophylactic antacids in severely stressed patients will also markedly reduce the incidence of bleeding gastritis. The concept of "no acid - no ulcer" originally coined in 1910, may thus carry over to the acute gastric mucosal lesion (183).

Three studies have been published evaluating the <u>treatment</u> of actively bleeding gastritis with antacids (184-186). Using frequent, large doses of antacid (60-180 ml. per hour) instilled through a nasogastric tube, bleeding was stopped for 5-6 days in 90% of the patients. Only mild diarrhea attended the use of antacids and rebleeding was rare. These were poorly or uncontrolled studies but offer an alternative to intra-arterial vasopressin where the drug or radiological support is unavailable. The logical extension of this form of therapy involves the new histamine H-2 receptor antagonists which reduce gastric acid secretion at the level of the parietal cell rather than neutralize. Early studies disclose effectiveness both in stopping and preventing bleeding from the acute gastric mucosal lesion (187,188).

Gastric Ulcer, Duodenal Ulcer, and Tumor

As opposed to the bleeding from Mallory-Weiss tears or the acute gastric mucosal lesion, bleeding from gastric ulcer, duodenal ulcer, or tumor is the result of chronic processes. If at all possible, then, patients with these lesions who do not respond to conventional therapy or who rebleed in hospital should be considered surgical candidates. In the few patients who are prohibitive surgical risks,or as a preoperative measure, however, it may prove beneficial to employ selective arterial catheterization. While the effectiveness of vasopressin in such cases has been minimal, *embolization of solid material* into the bleeding artery is a method clinically used by an increasing number of angiographers. First proposed by Rosch in 1972 (189), it has arrested bleeding in 90% of both gastric and duodenal ulcers in subsequent studies (191-193). The solid material used has been unmodified autologous clot; autologous clot treated with oxidized cellulose, aminocaproic acid, or thrombin; and, most recently, surgical gelatin (Gelfoam) (194). The advantages of this technique, if successful, are obvious but the disadvantages are such as to limit the technique to those centers with highly experienced angiographers. Several cases of gastric infarction (195), intestinal necrosis (190) or hepatic ischemia (193) have been reported. Extreme caution must be exercised so that emboli do not escape the single desired artery and the technique should never be used in conjunction with vasopressin. Figure 16 demonstrates a successful attempt at embolizing a bleeding duodenal ulcer.

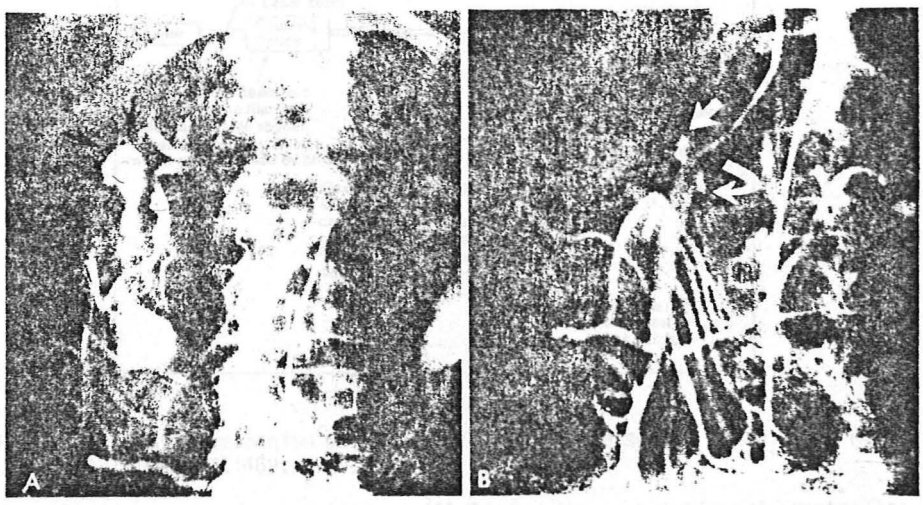


Figure 16. A. Extravasation of contrast material into a duodenal ulcer. B. Successful embolization of two branches of the gastroduodenal artery. From Athanasoulis C. Radiol. Clin. North Am. 14:265, 1976.

In this account of the tireless search for effective, safe methods of controlling UGI hemorrhage, pitfalls have been noted at every turn. Perhaps the most promising techniques yet proposed are the new *trans-endoscopic approaches* (196). Here would be a means of directly controlling the bleeding lesion at the same time the diagnosis is being made. These highly experimental means include the topical application of acrylic polymers (197), electrocoagulation (198-201), and laser beam thrombosis of the bleeding vessel (202-206).

Electrocoagulation has been used endoscopically in the removal of polyps for some time. Only recently have animal experiments been performed to determine the proper electrocoagulation settings for gastric mucosal hemostasis without full-thickness necrosis. Forty-six patients have now undergone this procedure, the largest series being that of Papp (201) who achieved cessation of bleeding in 95% of his cases without morbidity or mortality. Lesions successfully treated include all common sites of bleeding except esophageal varices.

Ketcham (202) demonstrated that a laser beam can produce small vessel thrombosis following which Goodale (203) showed that such therapy arrested gastric bleeding in dogs faster than electrocoagulation. This technique has now been applied to the flexible endoscope (204,205) (Figure 17) and the first successful result in humans has just been reported (206).

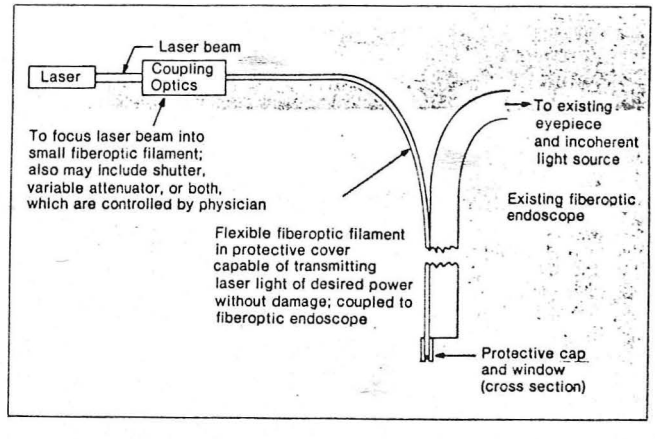


Figure 17. Laser mechanism adapted to flexible fiberscope. From Dwyer R. JAMA 231:489, 1975.

Whether these new modalities will live up to expectations in controlled studies may provide the nidus for another discussion of upper gastrointestinal hemorrhage several years hence.

A Philosophical Conclusion

To formulate a conclusion to this discussion is to be guilty of speaking a non-sequitor. Today's review of the newest in diagnosis and treatment of UGI hemorrhage has disclosed little more than promises and expectation. Surely, endoscopy and angiography have dramatically improved our ability to render an accurate diagnosis. Surely, endoscopy and angiography have fostered sophisticated approaches to treatment. What remains painfully unclear, however, is the degree to which these and other new modalities will improve patient well-being and survival. Until such information is forthcoming we can only hope to emulate those faculties exhibited in 1830 by Cruveilhier with his leeches and poultices - these attributes being common sense, impeccable observation, and employment of the most solid, basic means of patient care of our time. Granted, the latter has changed from blood-letting to intravenous fluids, blood transfusions, gastric lavage, and the judicious use of surgical intervention, but the basis is the same. Without such a firm framework, no technological advancement can hope to succeed.

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