Endoscopic Approaches to The Patient With UGI Hemorrhage

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I. Introduction

Physicians have been attempting for years to treat more effectively the patient with upper gastrointestinal (UGI) hemorrhage - for good reasons. Well over 150,000 patients are admitted to hospitals with this diagnosis each year in the United States.[1] The median duration of hospitalization for UGI hemorrhage is 7.5 days[2] and the average cost per day is between $300-400 in many hospitals. A conservative estimate, then, of the cost for UGI hemorrhage is $500,000,000 per year. Even more disconcerting is the fact that, despite improvement in the overall care of critically ill patients, mortality from UGI hemorrhage has remained at 10% for the past 30 years.[3-5] One possible explanation for this apparent dichotomy is that the age of the patient population is increasing and mortality from bleeding is especially high in the elderly.[3,4,6-8]

II. Endoscopy as a Diagnostic tool

The development of the fiberoptic panendoscope was hailed as a major breakthrough in the management of UGI hemorrhage. Here was an instrument which could accurately disclose the bleeding lesion, an event which would surely improve the care of the bleeding patient. As with many other modern diagnostic modalities (for example the CT Body Scanner), endoscopy became routinely and widely used without careful delineation of proper indications or solid evidence of its usefulness. This would not present a problem if endoscopy were proven to be safe, did not require both technician and physician time, and were free. Indeed, it is not unusual for an endoscopic examination to cost $300, which for 150,000 patients results in a yearly cost of $45,000,000. It is therefore of some importance to determine if routine endoscopy is justified in patients with UGI hemorrhage. In making this determination, we will consider separately two broad groups of patients. The first group consists of those patients with UGI hemorrhage who cease bleeding with routine resuscitative measures, (eg., fluid and blood replacement and gastric lavage). This group accounts for about 90% of all bleeders and is numerically the most important.[4] The other 10% are those patients who continue to bleed despite routine measures.

Endoscopy in Patients Who Cease Bleeding

The benefits one might derive from information obtained by endoscopy are shown in Table 1 as are the potential risks of the procedure. If endoscopy performed early-on in a patient's course could provide these benefits without the risks, one could easily justify its routine use.

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Table 1. Potential Benefits and Risks With Endoscopy

Benefits	Risks
Tailor immediate therapy	Pulmonary aspiration
Tailor long-term therapy	Arrhythmias
Shorten delay in care of rebleeder	Intestinal perforation
Shorten delay if surgery needed	Promote rebleeding
Improve short and long term mortality	
Shorten hospital stay	

From the outset, it is unlikely that endoscopy can help tailor immediate therapy in patients who cease bleeding. Table 2 shows the therapeutic options for each of the three main sources of UGI bleeding.

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Table 2. Immediate and long-term therapeutic options.

Lesion	Immediate Therapy	Long-term Therapy
Peptic Ulcer	Cimetidine or antacids	Treat 4-6 weeks/ consider surgery
Acute Mucosal Lesion	Cimetidine or antacids	Treat Reflux Symptoms
Varices	None	Therapeutic Portal Caval Shunt

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If a patient has a peptic ulcer (either gastric or duodenal) or an acute mucosal lesion (eg., Mallory-Weiss tear, gastritis, or esophagitis) he will be treated with cimetidine or antacids. If he has bled from varices, probably no immediate therapy is necessary. Thus one could merely treat all patients with cimetidine or antacids and feel comfortable. If endoscopy is to be of benefit, it must be via other means.

Certainly more plausible is the possibility that endoscopy can tailor long-term therapy. (Table 2) Patients with peptic ulcer would be treated for four to six weeks while patients with acute mucosal lesions or varices might not require such therapy. (One exception would be patients with persistent clinical symptoms of reflux esophagitis). Because antacids or cimetidine are safe and certainly less expensive than endoscopy, one could still make a case of treating everyone with antacids or cimetidine for a full six week course. Where long-term therapy would possibly be affected is if surgery is indicated. Patients with recurrent hemorrhage from peptic ulcer may require a definitive ulcer operation and patients with recurrent variceal hemorrhage a portal-caval shunt. However, the indications for these procedures are far from straightforward and, with varices, of uncertain benefit. When all is said and done, the only way to determine if endoscopy will provide these and other theoretical benefits is by a prospective controlled clinical trial. We have recently completed such a trial conducted over the past three years at the VA hospital.

Controlled Clinical Trial of Endoscopy
In Patients with UGI Hemorrhage

All patients at the Dallas VA Medical Center with acute UGI hemorrhage (Table 3) were entered into the study if they 1) stabilized within six hours of admission (Table 4); 2) had no contraindication to endoscopy (Table 5); ane 3) agreed to accept endoscopy if so randomized.

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Table 3. Criteria For UGI Hemorrhage

1. Hematemesis or melena with either guaiac positive stool or bloody nasogastric aspirate.
2. Hematochezia, anemia, or hypotension with a bloody nasogastric aspirate.

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Table 4. Criteria for Stabilization: Resuscitation with gastric lavage, fluid, and blood products results in:

1. Minimal active bleeding by nasogastric tube
2. No hypovolemia (defined as HR < 110, BP > 100 mm Hg, and no tilt (HR < 20; BP < 15)
3. Hct > 25%

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Table 5. Contraindications to Endoscopy

1. Uncooperative patient
2. Myocardial infarction
3. Severe pulmonary or myocardial insufficiency
4. Perforated viscus or signs of peritonitis
5. Dysphagia felt to be from a lesion in the proximal esophagus

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Patients were then randomly assigned either to undergo endoscopy within four hours of stabilization or not to undergo endoscopy. For reasons already discussed and to limit the variables, all patients whether endoscoped or not were treated similarly with a six-week course of antacids (one and three hours after meals and at bedtime). Every patient was scheduled for an UGI X-ray. Patients with a gastric ulcer found on X-ray (or on endoscopy in those patients so randomized) were treated with hourly antacids. Endoscopy was performed in patients randomized to no endoscopy only if recurrent hemorrhage occurred or the UGI X-ray was suspicious for a malignancy. All who survived hospitalization were followed in clinic for 12 months to determine long-term outcome.

206 patients were entered, 100 in the endoscopy (E) group and 106 in the no endoscopy (NE) group. The two groups were comparable in age, history and severity of liver disease, admission hemoglobin, the time required for stabilization, and the initial transfusion requirement. Seventy-five percent of the patients in each group required 2 or more units of blood transfusion. The source of bleeding in patients randomized to endoscopy are shown in Table 6.

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Table 6. Sources of bleeding in endoscopy group.

Gastric Ulcer	-	15%
Duodenal Ulcer	-	20%
Varices	-	20%
Mallory-Weiss	-	15%
Esophagitis/Gastritis	-	5%
Cancer	-	2%
Unknown	-	23%

* * * * *

While the great majority of patients bled from peptic ulcer, varices or a Mallory-Weiss lesion, only 5% bled from other acute mucosal lesions and 2% from cancer (one esophageal carcinoma and one lymphoma). It should be noted that both of these lesions were also diagnosed by UGI X-ray. Almost one-fourth had no clear diagnosis made, although in many instances the site of hemorrhage was noted. The hospital course of the patients in each group is shown in Table 7.

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Table 7. Hospital Course

	E(N=100)	NE(N=106)
Overall Mortality	11	8
Recurrent Hemorrhage	33	32
Time Until Recurrent Hemorrhage	2 days	3 days
Blood Needed for Recurrent Hemorrhage	6 Units	6 Units
Urgent Surgery	13	10
Time Until Urgent Surgery	5 days	4.5 days

* * * * *

It is clear that there is no significant difference in the outcome of a bleeding episode whether endoscopy is performed or not. Specifically, there was no important difference in mortality and the incidence or severity of recurrent hemorrhage. The sources of bleeding in those patients with recurrent hemorrhage are shown in Table 8.

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Table 8. Sources of bleeding in patients with recurrent hemorrhage.

	E(N=33)	NE(N=32)
Gastric Ulcer	4	8 (1 death)
Duodenal Ulcer	6	4 (1 death)
Varices	13 (7 deaths)	9 (3 deaths)
Mallory-Weiss	3	4
Acute Mucosal Lesion	3 (1 death)	2
Other	4	5

* * * * *

Delaying endoscopy until the time of recurrent hemorrhage did not delay urgent surgery. In the E group urgent surgery was required in 2 patients with gastric ulcer, 4 with duodenal ulcer, 6 with varices, and 1 with a possible stomal ulcer. In the NE group 5 patients underwent urgent surgery for gastric ulcer, 2 for duodenal ulcer, 2 for varices, and 1 for an arteriovenous malformation. 8 patients underwent elective surgery in each group. The major complication noted in endoscoped patients was pneumonia occurring in 4 patients in the E group and 2 in the NE group who had undergone endoscopy for recurrent hemorrhage. No intestinal perforations occurred. Hospital stay for patients with recurrent hemorrhage was 15 days in each group and in those without recurrent hemorrhage, 8 days in the endoscopy group and 9 days in the no endoscopy group.

The more interesting aspect of this trial lies in the long-term follow-up. Even if the immediate hospital course is not affected by endoscopy, there remains the fear that undiagnosed lesions in patients not endoscoped will prove troublesome during the ensuing months. Table 9 details the results of follow-up to date.

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Table 9. Twelve month follow Up Results

	E(N=67)	NE(N=66)
Re-Admission	14	14
Another bleeding episode	7	4
Surgery	3	4
"Bleed-related" death	2	3
Total deaths	7	12

* * * * *

Several points can be made from these data. First, randomization to no endoscopy did not result in a higher incidence of readmission to hospital for gastrointestinal problems in general or gastrointestinal hemorrhage in particular. Second, all three patients in the no endoscopy with "bleed-related" deaths had experienced recurrent hemorrhage during their original hospitalization and had therefore undergone endoscopy. Finally, the majority of deaths were the result of "non bleeding" phenomena.

Endoscopy in Patients Who Continue to Bleed

The employment of endoscopy would appear to be better justified in the smaller group of patients who continue bleeding because these patients present a therapeutic dilemma. As seen in Table 10, the immediate therapy for the three major groups of bleeding lesions is vastly different.

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Table 10. Immediate therapeutic options in patients who continue bleeding

Lesion	Immediate Therapy
Peptic Ulcer	Surgery
Acute Mucosal Lesion	Intra-arterial Pitressin
Varices	Intravenous Pitressin or Balloon Tamponade

* * * * *

If therapy is to be tailored to the particular bleeding lesion, it is obvious we must diagnose the lesion. Because of the ethical improprieties of treating such critically ill patients with the wrong therapy (for example, sending a patient to surgery with a non-surgical lesion), a randomized trial of endoscopy in this situation will probably never be performed.

Summary

Diagnostic endoscopy appears to play an important role only in those patients with UGI hemorrhage who continue to bleed despite resuscitative measures, although even in this situation there is no solid proof it affects patient outcome. Even if endoscopy in this situation has made an impact, it has not resulted in improvement in overall mortality. This may be the result of two factors. First, the group of continuing bleeders represents a numerically small proportion of patients with UGI hemorrage. Second, whatever benefit might be attributed to endoscopy may be masked by the fact that patients are older today and mortality from bleeding in general is higher in the elderly. If endoscopy is to have any further impact on the management of patients with UGI hemorrhage, it must be as a <u>therapeutic</u> tool.

III. <u>Endoscopy As A Therapeutic Tool</u>

Rationale

Mortality and morbidity associated with UGI hemorrhage is a reflection of the outcome in three groups of patients. First, there are patients who, because of underlying chronic disease (such as cirrhosis, severe heart or lung disease) and/or advanced age, will do poorly regardless of the severity or outcome of the bleeding episode. Second, there are patients with underlying disease in whom a severe bleeding episode tips the balance. Third, there are patients who simply exsanguinate. It is the latter two groups of patients in whom therapeutic endoscopy may play a role by reducing the severity of hemorrhage. Such a tool would be of particular help if it could prevent rebleeding episodes (which increases mortality) or could stop continuing hemorrhage quickly without the necessity of employing invasive and time-consuming procedures such as intra-arterial vasopressin or emergency surgery. The remainder of this discussion will dwell on endoscopically-deliverable therapeutic measures for UGI hemorrhage (Table 11).

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Table 11. Endoscopically Deliverable Forms of Therapy for UGI hemorrhage

<u>Non Thermal</u>	<u>Thermal</u>
Variceal injection	Heater probe
Topical thrombin	Electrocoagulation
Tissue adhesives	Laser photocoagulation

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Variceal Injection

The injection of a sclerosing agent into esophageal varices as a means of controlling variceal hemorrhage was first described 40 years ago but has received only modest attention in the medical literature.[9-12] The tip of an endoscope is used to distend a varix at the gastroesophageal junction. A needle is introduced into the varix itself and a sclerosant injected to obliterate the vein. (Figure 1A). The endoscope then is advanced to tamponade the vessel. (Figure 1B).

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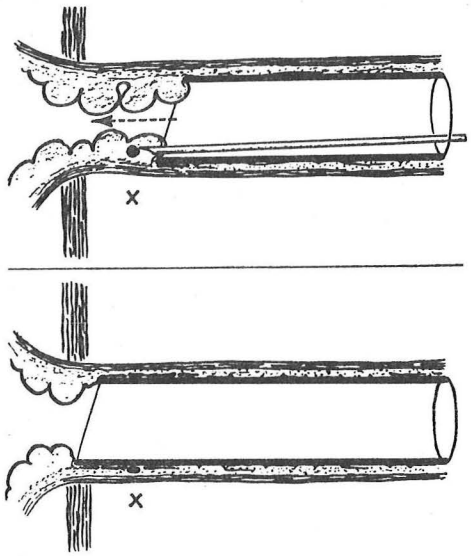
Figure 1.

A.

B.



The procedure is repeated until all varices are obliterated. Early, uncontrolled enthusiastic reports tell of 85-95% success in stopping bleeding although long-term follow-up has been sketchy. The complication incidence is about 10% and includes the inducement of hemorrhage from gastric varices, esophageal ulceration and perforation, and esophageal stricture. This technique is now applicable to the flexible fiberendoscope[12] and offers a possible alternative to more invasive means of controlling severe variceal hemorrhage (eg., emergency portal decompression or transhepatic obliteration of the coronary vein which feeds varices). As with any new procedure, it is mandatory to have strict guidelines for its use and to gather data systematically. If open trials show promise, controlled trials are indicated to determine its appropriate role.

Topical Thrombin

Linscheer and Fazio have recently published the results of a study in which thrombin and fibrinogen (as cryoprecipitate) were sprayed onto experimental ulcers in dogs.[13] (Figure 2) They used what has become the standard experimental ulcer model to test new approaches to the therapy of bleeding lesions.[14] The technique employs a suction biopsy apparatus modified by enlarging the capsule and its biopsy orifice (Figure 3). An acute gastric ulcer is made (Figure 4) which in heparinized dogs continues bleeding until exsanguination occurs or therapy is applied.

Figure 2. Spraying device (Medi-Tech). a) CO_2 pressure tank; b) 2mm diameter, 4 channel catheter; c) foot pedal; d and e) twin syringe with thrombin (5 ml) and cryoprecipitate (10 ml); f) saline syringe.

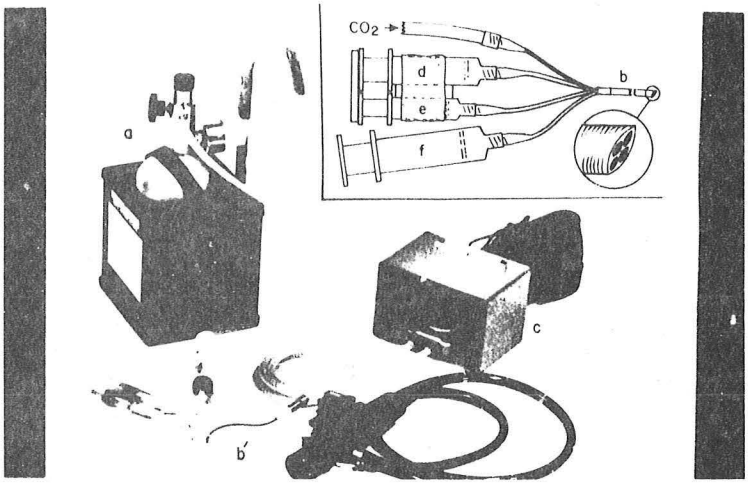


Figure 3. a) exploded view of the ulcer maker showing (left to right) the outer capsule with its biopsy aperture, cylindrical cutting knife, and internal oburator attached to the base of the instrument; b) the assembled ulcer maker with the cutting knife half closed in the biopsy port; c) diagram of the ulcer maker in use with gastric mucosa and submucosa sucked into the biopsy aperture before excision.

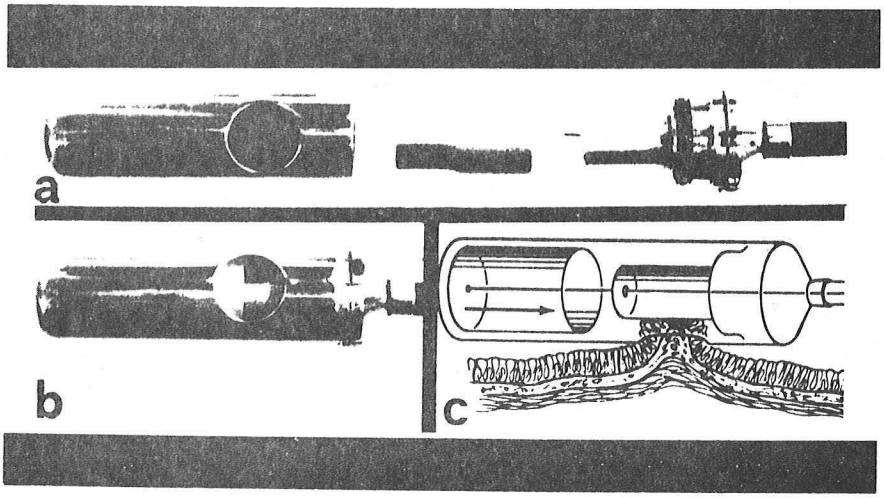
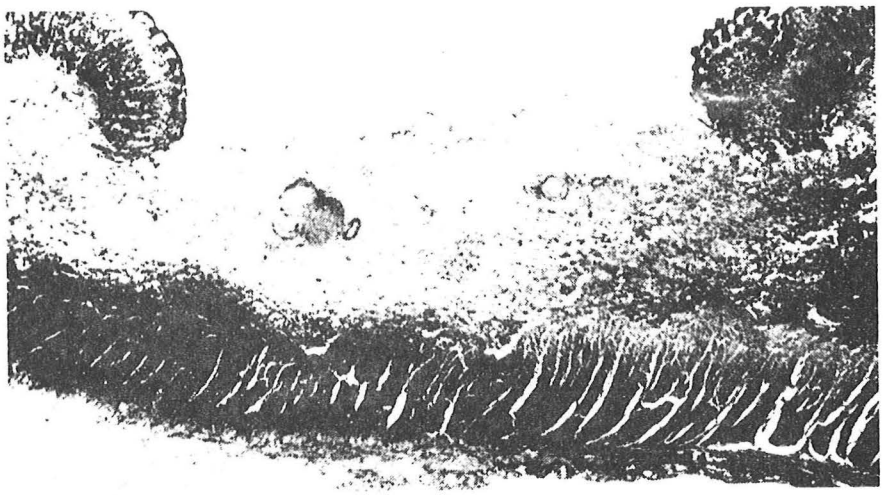


Figure 4. Typical acute gastric ulcer made by the ulcer maker. Note the prominence of vascular structures in the submucosa (X 9.2).



The thrombin - fibrinogen spray was more effective than control in both unheparinized and heparinized dogs. While a jet of CO_2 temporarily halts bleeding, a clot is formed almost instantaneously. The authors caution that this technique will be best applied to "slow oozers" rather than the more ominous "fast pumpers". Whether or not topical thrombin will be of clinical importance awaits a controlled clinical trial.

Tissue Adhesives

Cyanoacrylate plastic tissue adhesives (Figure 5) were orginally developed to treat battlefield wounds.

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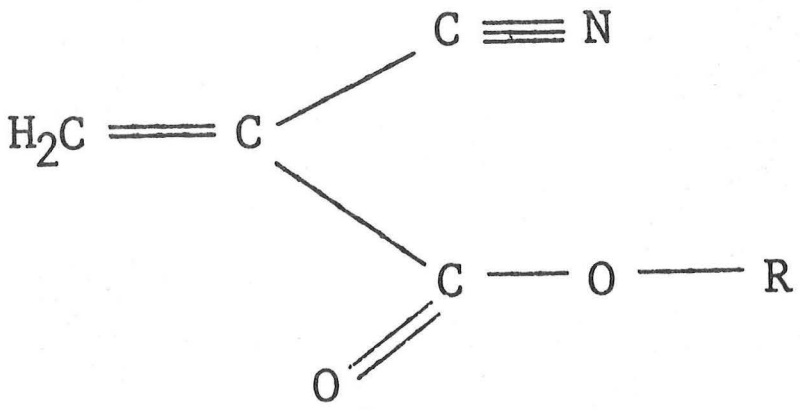
Figure 5. Cyanoacrylate monomer



These substances polymerize upon contact with moisture and can be applied as aerosals via an endoscope (Figure 6).

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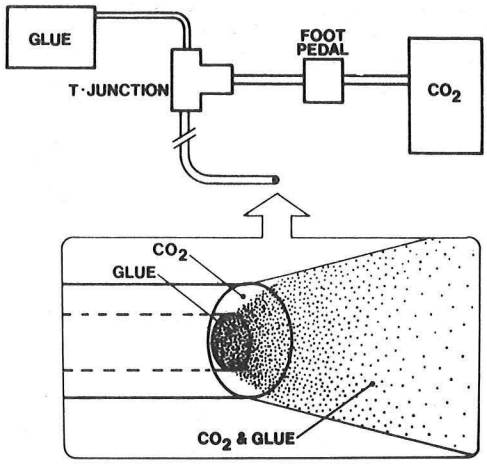
Figure 6. Schematic drawing of glue - CO_2 spraying system which can be passed through on endoscope.



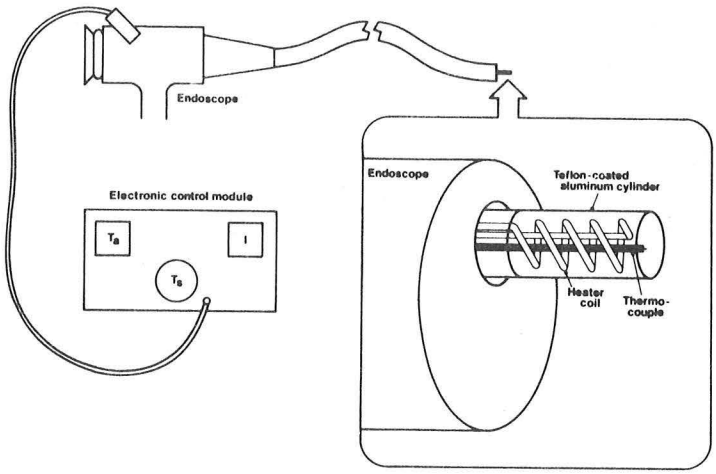
One derivative (the trifluroisopropyl analogue-Flucrylate - 3M) has been tested in the animal model described above.[15] None of twelve briskly bleeding ulcers were stopped with Flucrylate whereas 5/12 oozing ulcers were controlled. Thus, as with topical thrombin, this modality appears to have limited usefulness. Of note, however, Flucrylate produced no histologic tissue damage. A pilot study in humans has been reported.[16] Three of six patients were successfully treated with Flucrylate and in two of six bleeding was slowed. This was an uncontrolled study and, once again, must be confirmed by a sham-controlled clinical trial.

From the forgoing discussion, it appears that non-thermal measures are probably not the answer to control non-variceal UGI hemorrhage. Early results with thermal measures are more promising but also are potentially more dangerous than non-thermal methods. Depth of tissue injury occurring with thermal therapy therefore becomes an important aspect of the following discussions.

Heater Probe

The heater probe was designed to combine heat and pressure to control bleeding.[17] It consists of a heater element within a teflon-coated (to prevent sticking) aluminum cylinder. (Figure 7) The probe is applied to the bleeding lesion much like a hot iron.

Figure 7. Endoscopic heater probe (3.2 mm diameter).



A thermocouple in the tip maintains the temperature at the level (100-180°C) set on a control panel (Figure 8A). The Seattle group first designed a 6.4 mm diameter probe and then a 3.2 mm probe which could be passed through a flexible endoscope (Figures 8B and 8C).

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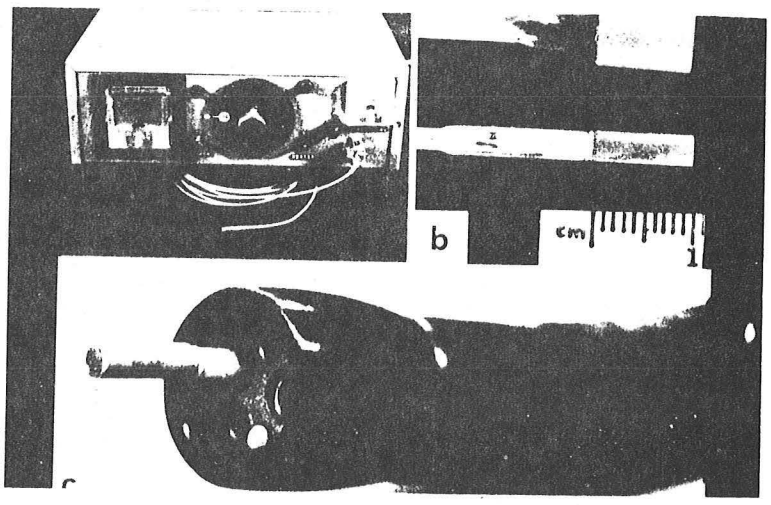
Figure 8. a) electronic control module with attached 3.2 mm diameter heater probe; b) close-up of heater probe tips: 6.4 mm diameter (above); 3.2 mm diameter (below); c) 3.2 mm diameter probe exiting from the biopsy channel of a standard endoscope.



Experimental ulcers were created and then either sham-treated or treated with the heater probe. Several dogs were sacrificed at various intervals after treatment and the ulcers examined histologically to determine depth of injury. Table 12 shows the effect of heater-probe therapy in stopping bleeding and the incidence of full-thickness tissue injury produced.

* * * * *

Table 12. Effect of heater probe on experimental ulcers.

Treatment	Cessation of Bleeding	Full-Thickness Injury
Sham	0/10	0/3
6.4 mm probe, laparotomy	12/12	7/18
3.2 mm probe, laparotomy	25/25	2/30
3.2 mm probe-endoscopy	18/19	6/19

* * * * *

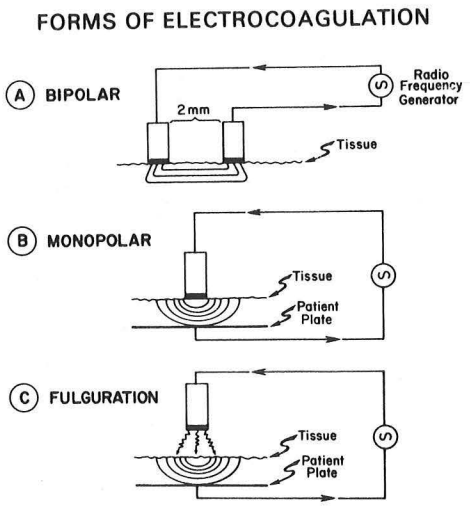
The heater probe was very effective in controlling bleeding, even when used via endoscopy. Tissue injury was unacceptably severe with the 6.4 mm probe but was much less with the smaller probe when used in the open dog stomach. Unfortunately, the 3.2 mm probe when used endoscopically produced full-thickness tissue injury in almost one-third of the treated ulcers. This technique, then, is not ready for testing in human subjects. However, attempts are being made to reduce the damaging effects of the heater probe by using coaxial CO_2 to remove overlying blood from the lesion, by regulating the pressure applied to the lesion, and by the development of a rapid turn-on, turn-off probe. If one or all of these make the heater probe successful, a thorough evaluation in patients can be conducted.

Electrocoagulation

Electrocoagulation occurs when radio frequency electrical current flows through tissue or blood. Resistance to electrical flow generates heat which coagulates by desiccation of tissue and denaturation of protein. It has been used non-endoscopically by surgeons for years to control bleeding (the familiar "Bovie") but has been recognized only recently as a potential means of controlling gastrointestinal hemorrhage via an endoscope.[18-22] To understand the development of electrocoagulation as a means of controlling bleeding, it is necessary to discuss briefly several engineering considerations.[1]

Electricity can be applied to tissue by either a bipolar or monopolar electrode. With a bipolar electrode, the electrical circuit is completed between two active electrodes, approximately 2 mm apart, touched directly to the tissue. (Figure 9A). A monopolar electrode transmits current through tissue to a reference electrode (or patient plate). The electrode may be placed directly on the tissue (Figure 9B) or held at a slight distance whereby a spark will jump the gap (fulguration, Figure 9C).

Figure 9.



Whether a current will fulgurate is dependent on the voltage applied. Whether the current will "cut" or "coagulate" is dependent on the waveform applied. Examples are shown in Figure 10.

* * * * *

Figure 10.

CURRENT WAVEFORMS

	Cut	Coagulate	Fulgurate
A	+	0	0
B	+	0	+
C	0	+	0
D	0	+	+

In Figure 10A, a low peak-voltage, continuous wave form will produce cutting but will not fulgurate. Figure 10B displays a cutting pattern that will fulgurate. Figure 10C and 10D display coagulating wave forms, the latter capable of fulguration. Although fulguration offers the advantage of no tissue contact, therefore avoiding adherence to the clot, it produces unacceptably deep tissue injury.[23] The current shown in Figure 10C is therefore what is used for coagulation of bleeding lesions.

Two other factors that play roles in the efficacy and depth of injury from electrocoagulation are the energy delivered and the force of application of the electrode.[24] The energy delivered to the electrode is a function of the equation:

Power (Watts) X Time (Sec) = Energy (Joules)

One can alter the energy delivered by changing the Wattage or the duration of application. For example:

Power		Time		Energy
10W	X	1 Sec	=	10 Joules
20W	X	1/2 Sec	=	10 Joules
20W	X	1 Sec	=	20 Joules
10W	X	2 Sec	=	20 Joules

For experimental purposes it is essential that energy delivered to the electrode be quantitated. To do this, the Seattle group devised a high-frequency electrical analog computer which can measure energy delivered or can deliver a pre-set level of energy.[24]

Energy delivered to the electrode is only one aspect of delivered energy. What one really wants to know is how much energy is delivered to tissue. This is a reflection of the area being heated and is expressed by the equation for energy density:

$$\text{Electrode Energy (Joules)} \times \frac{1}{\text{Area (cm}^2\text{)}} = \text{Energy Density (J/cm}^2\text{)}$$

An example of this relationship is shown in Figure 11. As the radius is doubled, there results a four-fold reduction in energy density. Two important determinants of energy density with coagulation electrodes are the area of the face of the electrode and the insulation of the electrode tip (Figure 12).

Figure 11.

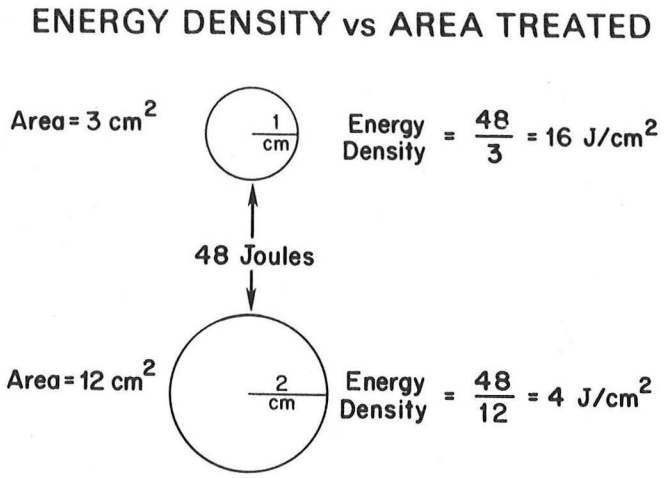
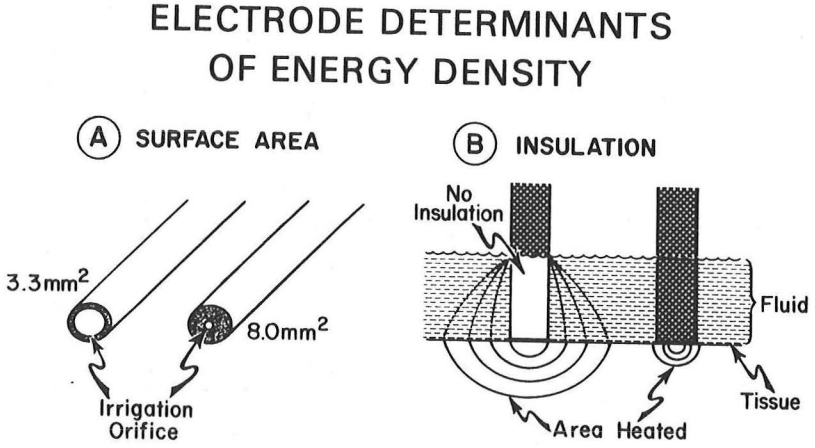


Figure 12.



By reducing the size of the irrigation orifice, the area of the electrode face is increased (Figure 12A), reducing the energy density, and possibly reducing tissue injury. On the other hand, the use of an un-insulated electrode allows the current to dissipate through fluid to cover a larger area (Figure 12B). In this case, the energy density is too low for effective hemostasis.

Finally, the force of application directly influences the depth of injury produced by an electrocoagulation electrode. Using a strain gauge to measure pressure, Silverstein's group determined the depth of injury produced by a monopolar electrode applied to dog stomach with a light (10 gm) or moderate (50 gm) push (Table 13).

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Table 13. Effect of pressure on depth of injury from monopolar electrocoagulation.

Force Applied	Depth of injury (% wall thickness)
10 gm	36%
50 gm	87%

* * * * *

Clearly, a heavy hand will lead to deeper injury.

After consideration of all of these engineering aspects, the inherent efficacy and potential for tissue injury of various electrodes were determined. Experimental ulcers were made as described previously and, using the same pressure and amount of energy to the electrode, three insulated electrodes were tested (Table 14).[25]

* * * * *

Table 14. Effect of three electrodes on experimental ulcers.

Electrode	Bleeding stopped/ Ulcers Treated*	Median Depth of Tissue Injury	Full Thickness Injury
Bipolar	15/17	30%	0/17
3.3mm^2 monopolar	20/21	60%	3/21
8.0mm^2 monopolar	21/21	60%	4/21

*Untreated control ulcers continue to bleed.

* * * * *

All three electrodes effectively controlled bleeding but the bipolar electrode produced less tissue injury and no full-thickness injury.

The monopolar electrode has been utilized in human subjects with a reported success rate of over 90%.[26-28] However, these are totally uncontrolled observations which must be confirmed by a controlled trial.

Laser Photocoagulation

LASER is an acronym for Light Amplification by Stimulated Emission of Radiation. This phenomenon, predicted by Einstein in 1917, occurs when a substance is taken to a high energy state and then stimulated to emit light when forced back to a low energy state by ambient radiation.[29] The resultant light is intense, monochromatic, and spatially coherent;

the latter property allows the light to be focused to a small point. When the light is absorbed by tissue or blood, heat is generated which coagulates blood and tissue protein.

When an atomic medium is "pumped" up to a high energy state by some external source of energy, it will undergo spontaneous decay. When it does so, depending on the medium chosen, photons of light will be emitted (Figure 13). This is the theory behind the neon lamp.

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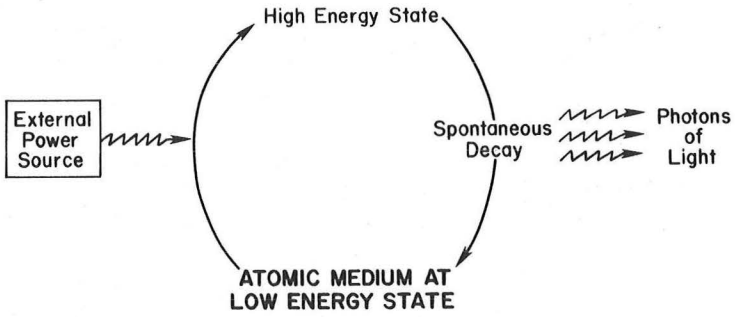
Figure 13.

SPONTANEOUS EMISSION
OF RADIATION

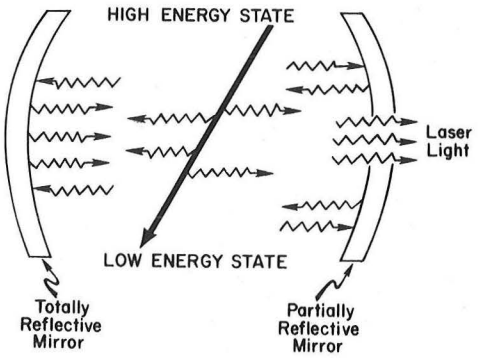


If one now places focused mirrors at each end of the tube containing the active medium, the photons released by spontaneous decay will oscillate very rapidly between them. In doing so, they greatly accelerate the decay of the active medium back to its low energy state resulting in the stimulated emission of monochromatic light.[29] (Figure 14)

* * * * *

Figure 14.

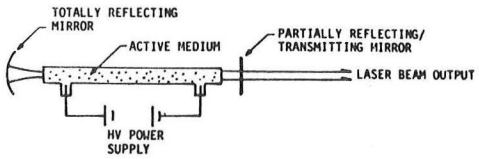
STIMULATED EMISSION
OF RADIATION



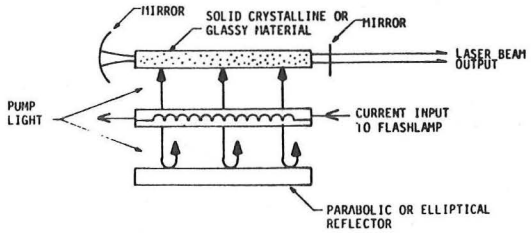
The light escapes the tube through one of the mirrors which is made partially transparent; when absorbed by tissue, the light generates heat. The first operational laser was built in 1960 by Maiman who used a ruby.[30] Since then, other substances have been utilized including gases (such as carbon dioxide and argon) and solids (such as neodymium). The medium can be pumped to a higher energy state either by a high voltage power supply (as with argon gas) or by a flashlamp (as with neodymium). (Figure 15).

Figure 15. Two typical laser cavities. A. Electron-collision-pumped gas laser. B. Optically pumped solid-state laser.

A.



B.



Ketcham first noted that laser-induced tissue heating produced small blood vessel thrombosis, making laser a potential means of controlling gastrointestinal hemorrhage.[31] To be clinically applicable, a laser must have sufficient energy to stop bleeding without causing perforation of bowel wall and must be able to be passed via a flexible wave guide which can be inserted through a fiber-endoscope. Goodale demonstrated in 1970 that a carbon dioxide laser could control bleeding from gastric erosions.[32] However, the carbon dioxide laser produces only very superficial hemostasis and is not spatially coherent enough to allow passage down a flexible waveguide.

The argon laser can be focused to a spot 10μm in diameter and as such can be delivered through a flexible fiberendoscope. German workers first demonstrated that this laser could control experimental ulcer bleeding in animals without causing severe tissue injury.[33-35] American investigators confirmed these results[36,37] and shortly thereafter the use of argon laser in human subjects was reported.[38-40] It became apparent, however, that the effectiveness of argon laser was limited in severe bleeding because the light is absorbed by red blood covering the lesion before reaching the underlying open artery. The reason for this is that argon produces a blue-green light (wavelength 0.5 μm) which is selectively absorbed by red. Two approaches were taken to circumvent this problem. Fruhmorgen[41] and Silverstein's group[42-44] devised a system whereby a jet of carbon dioxide gas coaxial to the laser beam removes overlying blood, slows bleeding transiently, and allows the laser's energy to be deposited on the bleeding vessel. Studies in animals demonstrated 100% effectiveness in stopping hemorrhage.

The second solution to the problem of absorption of argon laser light by red blood was the employment of laser of another wavelength, specificially neodymium in a matrix of yttrium aluminum garnet (Nd: YAG). The wave length of this laser (1.06 μm in the near infra-red range) is less well absorbed by red blood. In fact, this laser penetrates three to four times deeper in red than the argon laser. However, because the volume to be heated becomes proportionately larger (reducing energy density) there must be three to four times more energy delivered. Thus, while argon laser with coaxial carbon dioxide is used at a power of 7-10 watts, the Nd: YAG laser is used at 40 or more watts. Deeper tissue penetration with higher power makes the Nd: YAG laser more likely to produce deep tissue injury. The pioneering work with Nd: YAG was performed by Keifhaber.[45]

Comparative trials of argon laser with coaxial carbon dioxide and Nd:YAG laser have been performed in experimental animals by three groups directed by Silverstein, Jensen, and Waitman.[46-48] Their results are shown in Table 15.

* * * * *

Table 15. Comparison of Argon and Nd:YAG Lasers In Experimental Animals.

	Laser (Power)	Bleeding Stopped*	Percent Ulcers With Full-Thickness Injury
Silverstein[46]	Nd: YAG (55w)	100%	43%
	Argon (7w)	100%	10%
Jensen[47]	Nd: YAG (70w)	100%	79%
	Argon (10w)	100%	0%
Waitman[48]	Nd: YAG (80w)	100%	50%
	Argon (7.5w)	100%	0%

*Untreated control lesions continue to bleed.

* * * * *

It is clear that both lasers are effective. The Nd: YAG laser, however, produces a much higher incidence of full-thickness tissue injury as measured by post-mortem histological examination. Dixon has confirmed this incidence of full-thickness tissue injury with Nd: YAG but believes that, in dogs, much greater energy is required to actually perforate the serosal membrane of the intestinal wall.[49] Whether this discrepancy between the energy needed to produce full thickness injury and perforation is also true in human subjects is not clear, but based on animal data, argon laser appears to have a much greater margin of safety.

Uncontrolled trials of argon laser with coaxial carbon dioxide (Figure 16) and Nd: YAG laser have been conducted in humans (Table 16).[45,50-53]

Figure 16. Argon Laser with Coaxial CO_2 Via Endoscopy

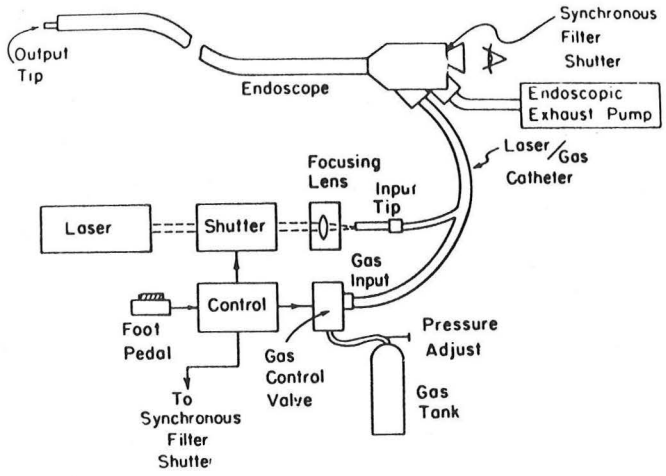


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Table 16.

Laser	Investigator	Bleeding Stopped/ Lesions Treated	Perforations
Nd:YAG	Kiefhaber[45]	106/110	2
	Dwyer[50]	52/58	2
Argon	Fruhmorgen[51]	96/100	0
	Waitman[52]	50/55	0
	Brunetaud[53]	10/10	0

* * * * *

As in the animal studies, both lasers are effective but the Nd:YAG appears to result in a perforation rate of 2-3%. Furthermore, these data are uncontrolled and, because the rate of spontaneous cessation of bleeding in untreated patients is unknown, it is impossible to assess efficacy. It is only through a controlled-clinical trial that clear-cut data can be obtained and because these techniques are potentially dangerous and, in the case of laser, very expensive, we believe it is essential that such a trial be performed. Hopefully, our group will soon direct an eight-center trial of argon laser and bipolar electrocoagulation. We will compare these modalities to sham therapy in patients with severe bleeding from gastric, duodenal, and stomal ulcer. If either technique proves effective, a valuable addition will be made to the therapy of UGI bleeding. If no efficacy is shown, these procedures can be discarded before they are widely and indiscriminately used.

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