THERAPEUTIC LASER ENDOSCOPY IN GASTROINTESTINAL DISEASE

DEVELOPMENTS IN GASTROENTEROLOGY

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THERAPEUTIC LASER ENDOSCOPY IN GASTROINTESTINAL DISEASE

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DEDICATION

This book is dedicated to A. Einstein who developed the theoretical concept of the laser and D. Vader who popularized its use.

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FOREWORD

The endoscopic use of lasers in the treatment of gastrointestinal diseases began within the last decade and has evolved rapidly. Work is now being done at more than 150 centers in Europe, the United States, Japan and the rest of the world. To date no publication has defined the state of the art. This text attempts to fill that void.

To disseminate information about therapeutic laser endoscopy, an increasing number of short courses have been sponsored in the United States wherein the attendee hears didactic lectures, views video tapes, and in addition, has the opportunity to have a "hands-on" experience with endoscopic laser therapy in the animal labs. This book is an expansion of the material presented in one such course sponsored by The Cook County Hospital in Chicago, Illinois, in October, 1982. The course was organized by Peter Bright-Asare, M.D., Chairman of Gastroenterology at the time of the course and chaired by Dr. Bright-Asare and myself. Some of the lectures from the course have been broadened and formalized. Other chapters were invited and added. Also included are group discussions about issues that are either controversial or undefined. Attempts were made to secure consensus opinion from experienced investigators in areas where no hard scientific experimental or clinical data exists.

The contributors have a wide range of interest and expertise. Dr. Charles Enderby of the Molectron Medical Corporation has a background in laser physics and has been intimately involved with the commercial development of laser in the United States. Dr. Larimore Cummins, who is currently practicing gastroenterology in Santa Cruz, California, has worked with Dr. Michael Nauenberg a laser physicist to develop a sophisticated computer program

which attempts to define laser-tissue interaction. The laboratory investigation of Dr. Dennis Jensen at UCLA evaluating both laser and non-laser endoscopic modalities for the therapy of gastrointestinal bleeding is generally regarded as some of the finest work done today. Dr. James Johnston, who was a collaborator of Dr. Jensen at UCLA, has now expanded his work into the setting of the community hospital in Jackson, Mississipi. Dr. Paul Rutgeerts from the prestigious Gastrointestinal Unit in Leuven, Belgium, has done extensive laboratory and clinical work with lasers. Dr. Peter Bright-Asare who leaves his position as Chief of Gastroenterology at Cook County Hospital to become Associate Dean of Research at Charles R. Drew Postgraduate Medical Scoool in Los Angeles is a newcomer to the field of lasers, but has published widely about the pharmacologic treatment of acid-peptic disease. Dr. Stephen Bown's work in London has been both in the laboratory and in humans. His unit has been the only one in the world to publish controlled clinical trials with both the Argon and Nd:YAG laser for treatment of gastrointestinal (GI) bleeding. Dr. Richard Dwyer's work in Los Angeles represented landmark activity in the United States. At about the same time that Kiefhaber in Munich and Dr. Fruhmorgen in Erlangen were reporting successful endoscopic laser therapy of GI bleeding Dr. Dwyer was doing the same in the United States. He now directs an exciting laser laboratory which studies cellular and subcellular effects of lasers as well as broader clinical applications. Dr. John Bowers, working with Dr. John Dixon at the University of Utah, has a large experience with lasers and has contributed significantly to the understanding of laser application in the lower GI tract. Dr. Gustavo Machicado is another member of the Los Angeles connection who has collaborated with Dr. Jensen. The creative work of Dr. Jean-Marc Brunetaud from Lille, France, has been exciting not only because of his inventive clinical applications, but also because of his contributions to the technical development of lasers. Dr. Arthur Klass who contributes to some of the panel discussions has been the gastrointestinal leader of laser application at Sinai Hospital in Detroit, Michigan, a center which has the most extensive multidisciplinary laser unit in America. Dr. Bergein Overholt, who currently is serving as president of The American Society of

Gastrointestinal Endoscopy, has been a leader in the progression of endoscopic development in the United States.

It is hoped this book will serve as a reference point for other work in the future.

David Fleischer

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A note of thanks to Dr. Bright-Asare's associates at Cook County Hispital, Chicago, whose hard work made the endoscopic laser therapy course that was the skeleton of this book so successful. This includes Mr. Paul Patterson, Ms. Yvonne Russell, Ms. Glenda Sanders, Ms. Gloria Grandberry, Mr. Ellsworth Hasbrouck, Dr. Robert Forrest, and especially Mr. Unis Pressley for his transcribing and audo-visual expertise.

In Cleveland the secretarial support of Ms. Madely Fellows and the administrative effort of Mr. Robert Crum were critical. Finally, the devoted concern and contributions of Ms. Ree Fuchs are simply to great to enumerate.

1. MEDICAL LASER FUNDAMENTALS

C. E. Enderby

This discussion presents the fundamentals of the interaction of lasers with biological materials. Included is a description of the different types of medical lasers, an explanation of the features that make lasers suitable for medical use, a discussion of basic principles of laser physics, and an assessment of the ophthalmologic safety of lasers to the physician.

The "heart" of any laser is the medium which forms the laser beam. This medium can be a gas, as found in a CO_2 or Argon laser, a liquid as in a dye laser or a solid material as in a Nd:YAG (Neodymium: Yttrium Aluminum Garnet) laser. Virtually anything can be used as a medium and made to lase. There was a university report several years ago in which Jello was made to lase. The different mediums must be "excited" to form a laser beam. (Fig. 1)

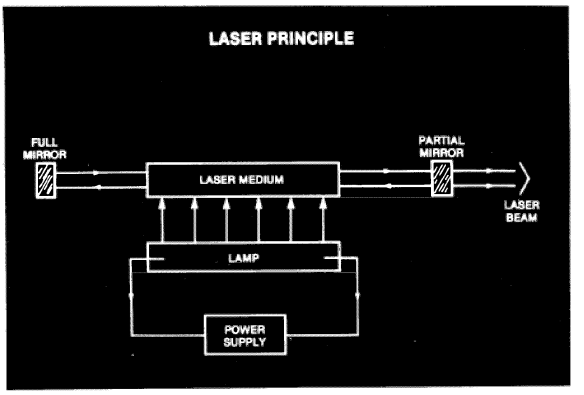


Fig. 1. Solid laser medium excited by an optical source

If the lasing medium is a gas, it can be excited with an electrical discharge. If it is a solid, a different energy source must be used, which in most cases, is an intense lamp. This lamp in turn is energized by an electrical power supply. The lamp transfers energy to the laser medium, part of which is absorbed by an active lasing element in that medium, i.e. Neodymium in the case of Nd:YAG lasers. The active element will then emit this energy spontaneously in the form of light. By placing mirrors outside of the laser medium, one at each end, some of

this spontaneous light is trapped and reflected back through the medium. When the light is reflected back through the laser medium it stimulates more of the excited atoms to release their excess energy, thereby increasing the intensity of the light. This continuous reflection and stimulation is where the acronym "LASER" comes from, Light Amplification by Stimulated Emmission of Radiation. By making one of the mirrors a partial reflector some of the light is transmitted through it, and is the laser beam.

Laser beams are useful in medicine because:

1. The laser beam is monochromatic, with a single wavelength interaction with tissue being predictable.
2. Laser light is coherent in both time and space. Which means it can be very intense and can be focused on to a small area. Laser light may be transmitted through fiber optical systems which in turn can be placed through an endoscope allowing the light to reach a treatment site.

Many types of lasers are used in medicine today. Due to their characteristics there are three which are most widely used. Namely Argon, CO_2 , and Nd:YAG lasers. (Fig. 2)

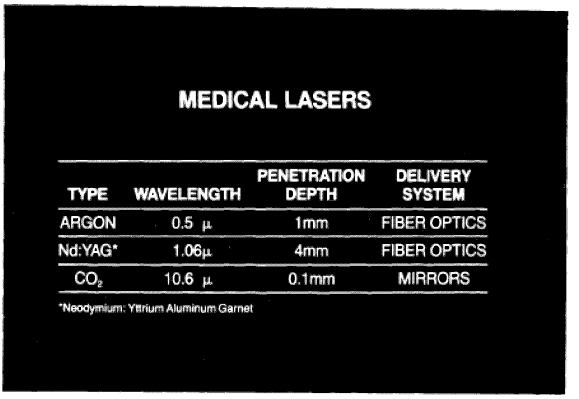


Fig. 2. Medical lasers commonly used

Other lasers used in medicine, on a more limited basis, are Krypton, Helium-neon, Ruby and Dye Lasers. Krypton is used in ophthalmology. Helium-neon is used as an aiming beam and also in acupuncture. Dye lasers have been used to excite photo sensitive materials such as hematoporphyrin deriviative. Ruby lasers were used in ophthalmology until Argon lasers replaced them.

The CO_2 laser operates at a wavelength of 10μ which is in the far infrared region of the electromagnetic spectrum, and therefore is invisible to the eye. The Nd:YAG operates at 1.06μ which is the near infrared and is also invisible. The Argon laser operates at 0.5μ which is in the visible blue-green region of the spectrum.

An important factor in the medical use of lasers is the delivery system. Fiber optics are used for both Argon and Nd:YAG lasers. There are now fibers available for the CO_2 laser, however they are not being used endoscopically because of their size and because they are made of toxic materials. They can be used to replace the mirrored articulated arms used on microscope attachment and handpieces. The application of these three lasers are different due to the penetration depth of the beam. (Fig. 3)

PRINCIPLE USES OF MEDICAL LASERS

LASER	ACTION	FIELDS
Argon	Coagulation	Opthalmology, Gastroenterology, Dermatology
Nd:YAG	Coagulation	Gastroenterology, Urology, Neurosurgery
CO_2	Ablation	Gynecology, Surgery, Otolaryngology

Fig. 3. Principle uses of medical lasers

The CO_2 laser is a vaporization laser which ablates tissue making its primary application in surgery and gynecology. The Nd:YAG is a coagulator with its primary application in the treatment of hemorrhage and tumor ablation. The Argon laser is also a coagulator with less penetration depth making it ideal in the field of ophthalmology.

The different interaction of these lasers is largely due to two materials found in biological tissues, water and hemoglobin. Absorption varies with the wavelength for each material. Hemoglobin has a high absorption of light at low wavelengths and has a low absorption in and passed the red region. Water has a high absorption for long wavelengths and a low absorption in the visible range. The Argon laser, therefore, has a high absorption in hemoglobin and negligible absorption in water. The CO_2 laser has a high absorption in water and low absorption in hemoglobin. The Nd:YAG laser

has some absorption in both hemoglobin and in water. (Fig. 4)

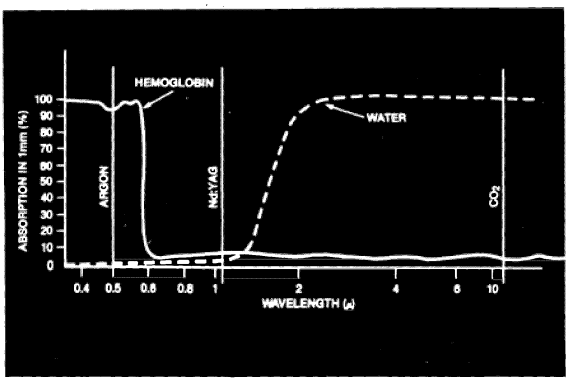


Fig. 4. Wavelength range and absorption of the CO_2, Argon and Nd:YAG lasers

Another important consideration is that of scattering. As the laser beam penetrates tissue some of that energy is scattered. Initially this scattering occurs at the surface, but some does occur internally. When a laser beam enters tissue it may be scattered in many directions, then be absorbed or rescattered. Tissue interaction is more than just a straight line projection. (Fig. 5)

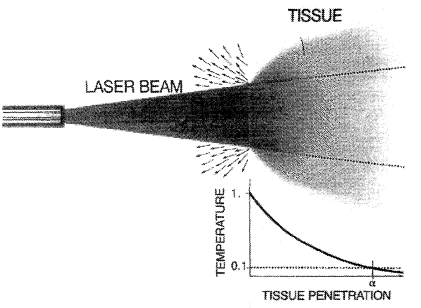


Fig. 5. Tissue penetration vs. temperature

Penetration is measured as the depth at which the energy level is only 10% of the initial energy level. The Nd:YAG will penetrate about 4mm into tissue. At 4mm the total amount of energy remaining is about 10% of the incident energy. For Argon this point is attained at about 1mm and for the CO_2 at about 0.1mm.

In the coagulation process there are three basic elements:

1. Tissue edema, which is the rupture of cells which provides a mechanical pressure on vessels thereby reducing their size

and blood flow.

2. Vessel shrinkage, where the collagen shrinks and blood flow is curtailed.
3. Protein denaturization of the blood forming a clot.

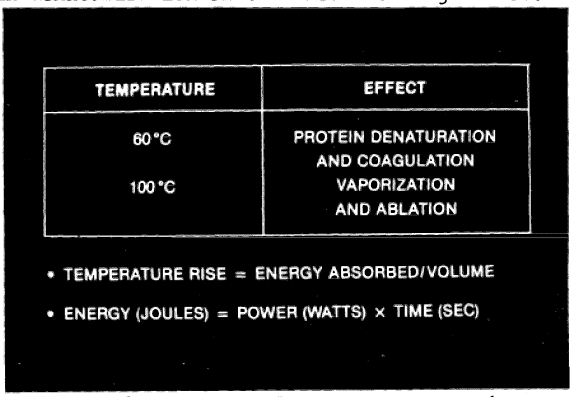


Fig. 6. The effects of temperature on tissue

Temperature is related to the amount of energy absorbed in a given volume. The volume affected is determined by the penetration depth and by the initial size of the beam. Energy is the amount of power that is absorbed during a period of time. These three factors, time, power, and volume determine the amount of energy, and therefore the temperature at the treatment site. Time and power can be controlled with the instrument while volume depends on the initial beam size, depth of penetration and scattering. Since the beam is emitted from the tip of the fiber at a diverging angle (usually 4 to 10 degrees), the beam or spot size on the tissue depends on distance of the fiber tip from the tissue (Fig. 7).

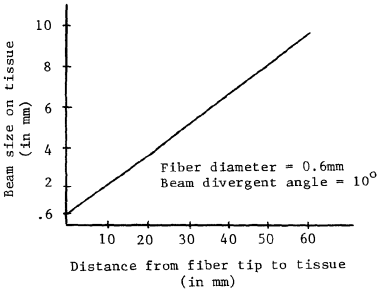


Fig. 7. Beam size on tissue vs. distance from fiber tip

The longer the distance, the larger the spot, and therefore the greater the volume affected. Other factors that must be taken into account for determination of tissue temperatures are:

1. Gas or water used at the treatment site to clear away blood or debris.
2. Blood flow through vessels in the tissue. Moving blood transports heat and has a cooling effect.

Blood flow is a vital consideration in the temperature change of the treatment site and one for which there is little direct control. The amount of blood flow may require changes in the power or time setting of the laser. The more blood flow the more power or faster delivery time may be required to achieve the desired temperature. Water or gas will act to cool down the tissue thus requiring an increase in laser power to attain the necessary temperature. The amount of power needed, the beam size, and exposure time required, varies for each application. Experience largely dictates what will work best. Since lasers are still in the investigational stage there are no set answers as to what works best. As experience increases some general rules "may" be formulated for the best techniques to apply for different treatments.

Medical lasers are well constructed, with reliability and ease of operation being of primary importance. Laser systems must produce the desired power and time setting accurately, and repeatably. Controls should be easy to operate and have no ambiguity. (Fig. 8)

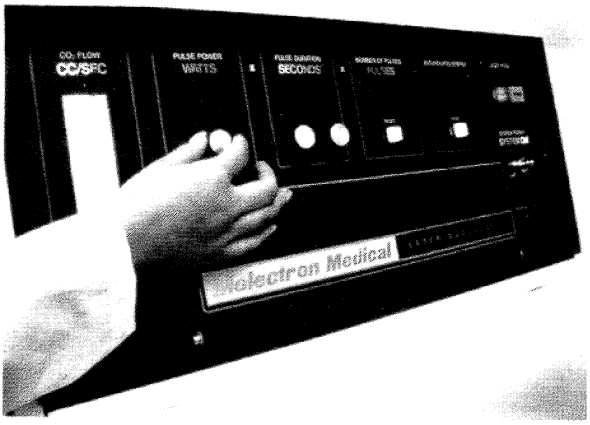


Fig. 8. Controls of a Nd:YAG laser

Frequently, in order to obtain accurate power readings, a separate power meter is built into the system which verifies the power output. The internal construction of the laser system must be extremely solid to prevent misalignment due to movement. A kinematic deck may be used to support the optics which prevents continual alignment problems. The electronics should be segregated from the water cooling system to prevent damage due to potential leaks.

Ophthalmic safety is important. A laser beam striking the eye may cause considerable damage, depending upon its intensity. The CO_2 laser can cause damage on the cornea surface due to the absorption of water. Exposure to the Argon and YAG lasers could cause damage to the retina, which can cause blind spots in the vision. Safety glasses and filters must be used. These are made of a material that absorbs the particular wavelength of laser light being used. For CO_2 lasers ordinary glass can be used. In the case of an Argon laser, the filter material is orange, which blocks the blue-green light of the Argon laser. Since this filter will color distort the view, it is mechanically put in place during the actual firing of the laser. In the case of the YAG laser, the filter material is almost clear in the visible spectrum, and can be left in place. Vision is not impaired with this filter in place.

The ophthalmic safe levels has been determined by the American National Standards. (fig.9)

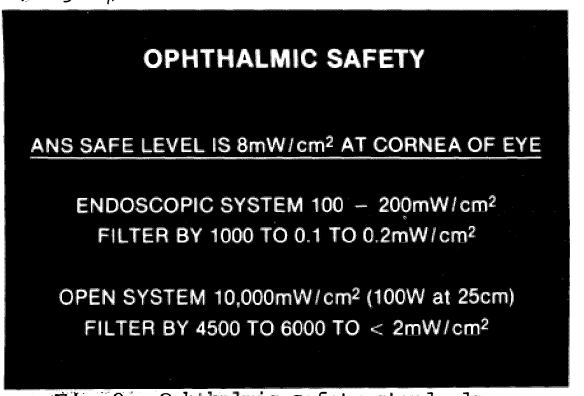


Fig.9 Ophthalmic safety standards

Studies have shown that for typical treatment levels with a Nd:YAG laser the reflected light from the mucosa up through the endoscope can be in the order of 100 to 200mW/cm^2, thereby requiring the use of a filter over the

ocular of the endoscope. The filters typically have attenuations of about 1,000 putting the reflective light well below the hazardous level. In an open system the eye could be exposed to the entire laser beam thereby requiring the use of safety glasses.

During the last 10-15 years lasers have been extensively used as a therapeutic tool. There are now hundreds of physicians, world wide, who use lasers on a regular basis. More research is required to measure the full potential of lasers and the various applications for which it will be best suited.

2. LASER TISSUE INTERACTION

L. Cummins

God said "Let there be light." Thus was provided the substrate from which arose the laser. The intervening eons saw an awesome accumulation of knowledge which was required to make laser light available to us. In the few years since this discovery we have experienced an explosive growth in our understanding of the effects and utility of this amazing form of electromagnetic radiation. The laser has provided yet another tool in the increasingly technichnical field of medical therapy. An appreciation of the basic events of laser tissue interaction will undoubtedly translate into more practical information for the laser therapist. We truly stand on the shoulders of giants as we review these events over the next few pages.

Laser tissue interaction can be viewed as occurring in three phases: the absorption-scattering phase, the heating phase and the cooling phase.

LIGHT ABSORPTION AND SCATTERING

The specifics of laser light generation have been explained in Chapter 1. We must answer several key questions regarding the interaction of laser light and biological tissue: How does light cause heat? What determines the distribution of light intensities throughout laser irradiated tissue? What are the physiological and anatomical effects of heat? What is the distribution of laser-generated heat and what happens to this thermal energy?

Let's first look at light and see how it causes heat. Figure 1 demonstrates three forms of light striking a plane in space. Three different wavelengths are depicted. All forms of light travel at the same speed and therefore the fluctuations in

electromagnetic energy as viewed from a single point in space will vary more rapidly with light of shorter wavelengths than light of longer wavelengths. Thus we have a relationship between frequency and wavelength. A rather crude translation from wave theory to quatum theory would equate light of shorter wavelength and higher frequency with photons arriving in larger numbers at a

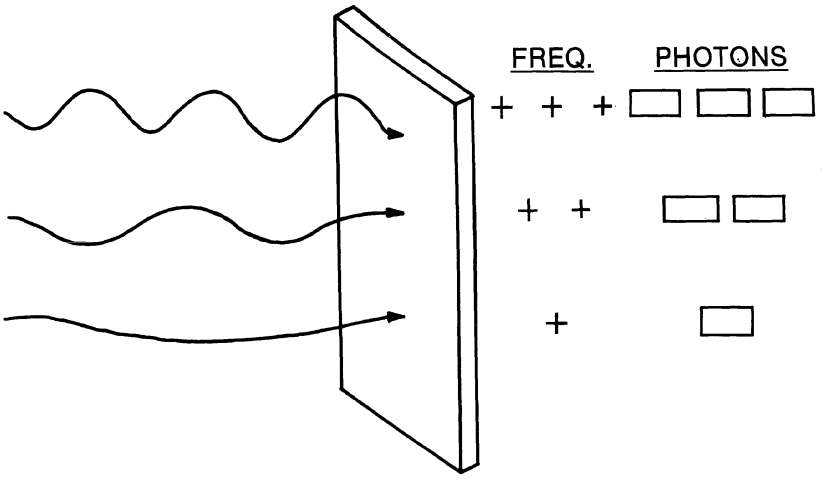


Figure 1. Light wavelength related to frequency

given point in space over a specified time interval. This translation would find objection from physicists who would remind us that photons are more complexly related to the frequency wavelengt and amplitude of electromagnetic radiation. However, this simple translation remains educational for clinical purposes. Different wavelengths mean different frequencies. Within a molecule there occur repetitive events which have their various frequencies of repetition (such as electrons orbiting and chemical bonds vibrating). Whether light is absorbed or scattered as a result of entering the molecular environment is determined in large part by matching of the light frequency with the frequency of one of these recurrent events.

There are certain characteristics of laser light which make it unique. A laser generator converts light of multiple wavelengths into light of the same wavelength. Such monochromatic light is depicted in the middle drawing of Figure 2. Light of mixed wavelength is represented by the drawing at the top. The lower drawing demonstrates the concept of coherence. The laser generator not

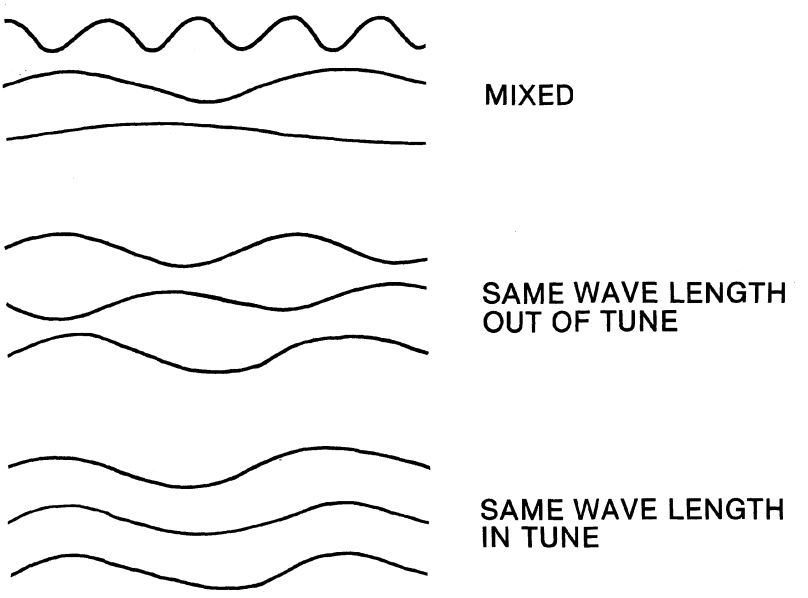


Figure 2. Laser light is monochromatic and coherent

only produces light of only a single wavelength, but also superimposes all of the electromagnetic waves such that they coincide in timing and in parallel direction. Thus laser light is special because it is monochromatic and coherent. These characteristics make the laser a unique and effective tool in medicine. Its parallel rays provide rifleshot accuracy and its monochromicity allows chemical specificity at the target site. Its coherence

provides that relatively large energy bursts can be delivered in small time-space units.

What is heat and how does light cause heat? Heat is random molecular movement. Consider the three containers of water in Figure 3. On the left we are reminded that water molecules do not simply stay put. They bounce around in a random Brownian

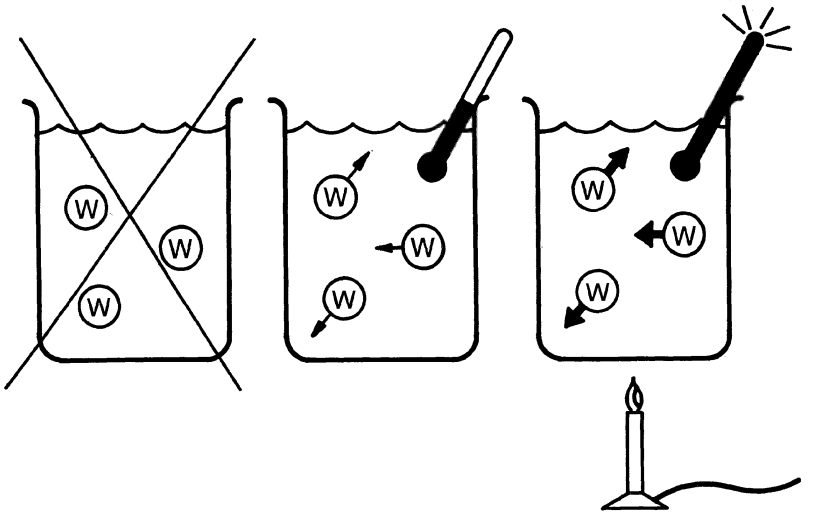


Figure 3. Thermal energy

fashion as suggested in the center drawing. This random molecular movement is directly related to the temperature of the water. Wher the water is heated, as depicted on the right, molecular agitation occurs and this is manifested by a rise in measured temperature. As demonstrated here, we are adding thermal energy with the use of a Bunsen burner, and its presence is manifested by molecular agitation. The reverse process is also valid. If we can create molecular agitation we have heat. They are essentially one and the same. We can create molecular agitation with laser light.

Direct frequency matching with molecular movement occurs when we heat a bowl of soup in a microwave oven. The only difference with laser light is that its frequency corresponds with subatomic events such as electrons spinning, orbiting, and dashing between energy levels. Just how these subatomic oscillating frequencies are translated into random molecular agitation (i.e. heat) is a matter for the nuclear physicist and is beyond the scope of this discussion. This rather simplistic concept of frequency matching versus heat is well suited to the level of understanding helpful to the clinician.

There are many nonthermal effects of electromagnetic irradiation. Most of these effects occur at much higher energy levels and frequency ranges than are available on the continuous wave laser generators in current clinical use. These non-thermal reactions include shattering of covalent bonds as well as weaker atomic associations. Free radical production and ionization can also occur in response to other forms of electro-magnetic radiation, but not laser light as described here.

Another concept which is fundamental to the understanding of laser tissue interaction is light scattering. We have thus far been referring to light absorption. We might now ask what happens if our frequencies almost match but not quite? The answer is that the photon bounces off the molecule. It is deflected around within the tissue until it is either absorbed or exits the tissue. This non-absorptive interaction is called scattering. When a photon enters biological tissue it can only do one of two things. It is either scattered or absorbed. Figure 4 graphically demonstrates these two options. Absorption is suggested by the small heat wave on the left, and scattering in one of four directions is suggested on the right. Note that the light can be scattered in any direction. Other terms such as reflection and transillumination might be used for back scatter and forward scatter respectively. Regardless of the terminology the basic process can be viewed as light scattering. Obviously factors such as angle of incidence and tissue layer interfaces will influence this process of scattering. For a given substance, light of a specific wavelength will have a unique absorption coefficient and

scattering coefficient. These values are determined experimentally by measuring the amount and direction of light scattered when a

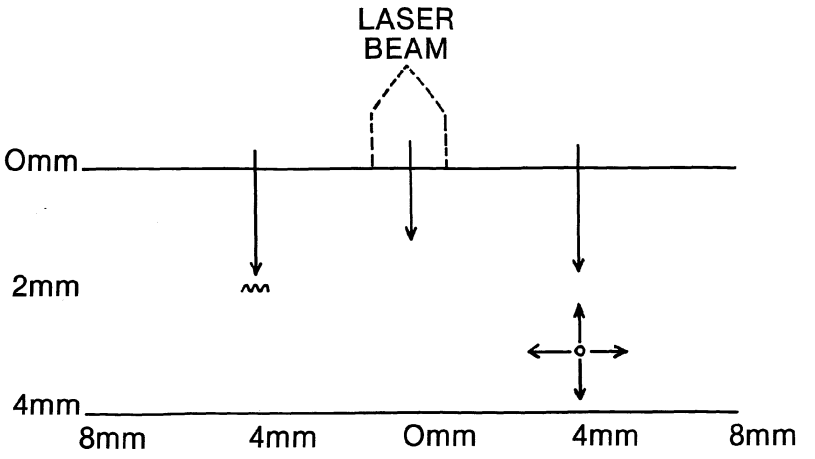


Figure 4. Laser light is either absorbed or scattered

substance is irradiated. The amount of light absorbed is measurec by the temperature rise within the experimental specimen. A rather crude measure of laser tissue interaction is the extinctior coefficient which is a statement of how rapidly light is extinguished as it penetrates the tissue. It includes both scattering and absorption however and does not distinguish between the two. Examples of experimentally determined absorption, scattering and extinction coefficients for various tissues are listed in Table 1

We can view tissue as an aqueous environment which always has plenty of water but varying amounts of protein, lipids and hemoglobin. It also has higher order structures such as cells, tissue layers, and blood vessels. Because of its remarkably high absorption in water the light generated by a CO2 laser is very effectively absorbed when it enters biological tissue. When making theoretical calculations of CO2 laser radiation, it is

assumed that all of the light is absorbed and none is scattered. This is in contrast to the neodymium:YAG laser, a photon of which

Nd:YAG Laser Absorption (a) and Scattering (b) Coefficients

	a	b	a+b	Source
Water	0.1			(8) Hofstetter
Blood	4			(8) Hofstetter
Bloodless urinary bladder	0.11	9.89		(6) Halldorsson
Mammalian stomach			5.7	(10) Kiefhaber
Mammalian liver			12.5	(10) Kiefhaber

Table 1. Absorption and scattering coefficients

is ten times more likely to be scattered than absorbed. Argon generated laser light is scattered and absorbed with equal probability in tissues of average water and hemoglobin content. These characteristics of the three lasers in clinical use result in very different patterns of light distribution within irradiated tissue. We can more closely examine this wavelength dependence using a computer generated simulation of laser tissue interaction.

Figure 5 illustrates a theoretical piece of tissue which is 4 mm. in thickness. Within the tissue are plotted the isointensity lines for 90% extinction. That is to say these lines connect all points in the tissue at which the light intensity is one tenth of the intensity impacting at the surface. The difference between the extinction profiles for the various lasers is strictly related to wavelength. It is apparent that the energy delivered by the neodynium:YAG laser will be distributed in a much larger tissue volume

than that of the CO2 laser. The Argon laser is intermediate in this respect. These isointensity distributions are represented as a percent of the incident laser beam. Regardless of how the

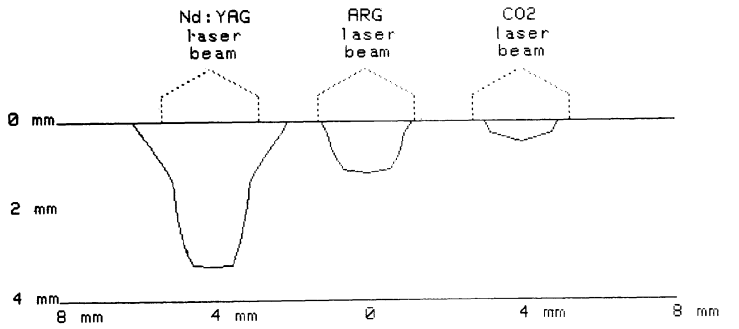


Figure 5. Ninety percent extinction profiles

laser is exposed to the tissue or how much power is applied these distributions will remain unchanged. The only factors other than wavelength which will influence this relative extinction profile are tissue constituents and therapeutic spot size. For a given spot size the actual intensities of light (as opposed to relative intensities) throughout the tissue will be determined by the power setting of the laser generator.

Thus we have described the first phase of laser tissue interaction, the absorption-scattering phase. Within the first picosecond after laser light contacts tissue an intensity pattern is established based upon the light wavelength, tissue constituents, therapeutic spot size and power setting. The latter two factors combined are frequently referred to as power density. For purposes of explanation they are separated here because they are

independent therapeutic variables available for manipulation by the clinician.

HEATING

The next phase of laser tissue interaction involves heating. This process follows a spacial pattern determined by the intensity profile established in the first phase. Again, the computer will help us understand the events of this heating process.

The computer visualizes the tissue as a two dimensional numerical matrix as would be represented by a piece of paper with 32 columns and 16 rows of numbers. Each number represents a point within the tissue each of which is 0.5 millimeters from its neighbor. Before the laser is fired, the computer assigns a temperature of 37 degrees centigrade to each point in the matrix. Each point has its own absorption and scattering coefficients as well as its own specific heat and thermal diffusivity. When this numerical matrix is extended into a third dimension, it is capable of representing all of the anatomical and physiological characteristics of tissue including blood vessels containing flowing blood and tissue layer interfaces. When laser light impacts upon the tissue surface with a given power setting and spot size the computer calculates the intensity of light at each and every point within the matrix. Based upon time of exposure and regional variations in absorption and thermal diffusivity, the computer then calculates an incremental temperature increase for each point within the tissue. As the temperature of the tissue rises its photoreactive characteristics change and the computer continually updates the tissue characteristics.

If we look at a thermal profile within our theoretical tissue, we encounter some of the important variables which are available for manipulation by the laser therapist. Let's look first at the neodymium:YAG laser. Figure 6 depicts the pattern of heating within tissue after a 3 second pulse of 80 watts with a therapeutic spot size of 2 mm. Plotted within the tissue are isothermal lines representing 40, 60, 80, and 100 degrees centigrade. Most proteins coagulate at approximately 60 degrees

centigrade, and thus the 60 degree isotherm represents the minimum extent of a laser lesion if histological preparations were made immediately after such a pulse. Additionally, water boils at 100 degrees, thus all of the tissue above the 100 degree isotherm would have been vaporized. This isotherm then becomes the new

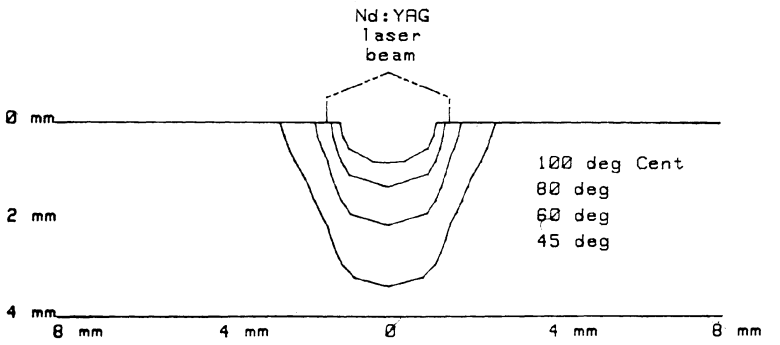
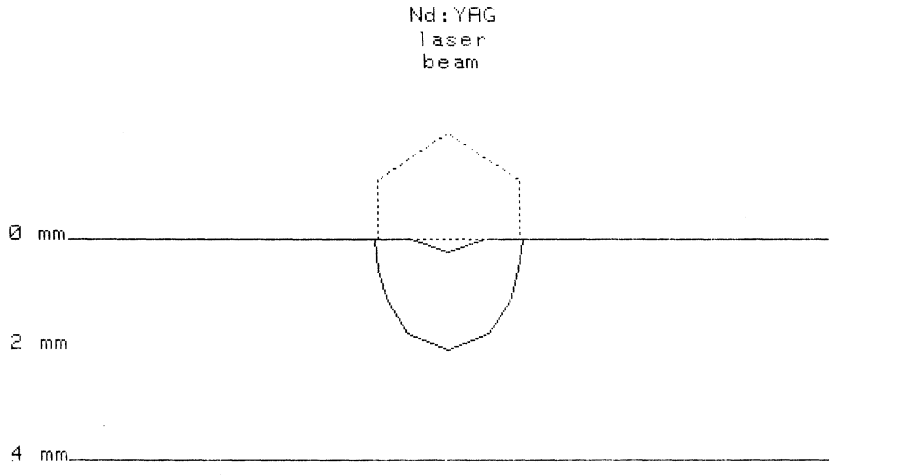


Figure 6. Theoretical isotherms within lasered tissue

tissue surface. You can see in Figure 6 that the computer has made a small divot in the tissue surface. If we asked the computer to continue shining the laser long enough, we would eventually see a hole burned through the theoretical tissue. Figure 7 is the computer's representation of a histological lesion by simply plotting the 100 degree isotherm as the new tissue surface and the 60 degree isotherm as the minimum extent of the histological lesion. Cell death and inflammatory changes extending beyond the coagulation zone would be expected to alter the lesion over time.

Using either this theoretical model or a dog's stomach, we can start to appreciate how variations in therapeutic parameters affect the laser lesion. In Figure 8 the result of increasing

the power of the laser beam is seen. Figure 9 demonstrates the



PULSE#	SPOT	PAUSE	POWER	DUR'N	PULSE ENERGY	TIME-ADJ PULS NRG	TOTAL ENERGY	TIME-ADJ TOTL NRG
1	3.0	0.00	100	1.25	125	125	125	125

Figure 7. Theoretical histology

effect of increased pulse durations and Figure 10 reveals the significance of therapeutic spot size.

COOLING

We have been dealing thus far with the events associated with a single pulse of laser light. Therapy for gastrointestinal bleeding almost always involves the delivery of multiple pulses to a rather broad area of tissue surface over a considerable period of time. There is a continuous process of tissue cooling which represents the third phase of laser tissue interaction. The term "phase" used here does not imply a time sequence but rather a conceptual dissection of the process of laser tissue interaction. For practical purposes all three phases begin at the same time. The absorption-scattering and heating phases continue throughout the duration of the laser pulse whereas the

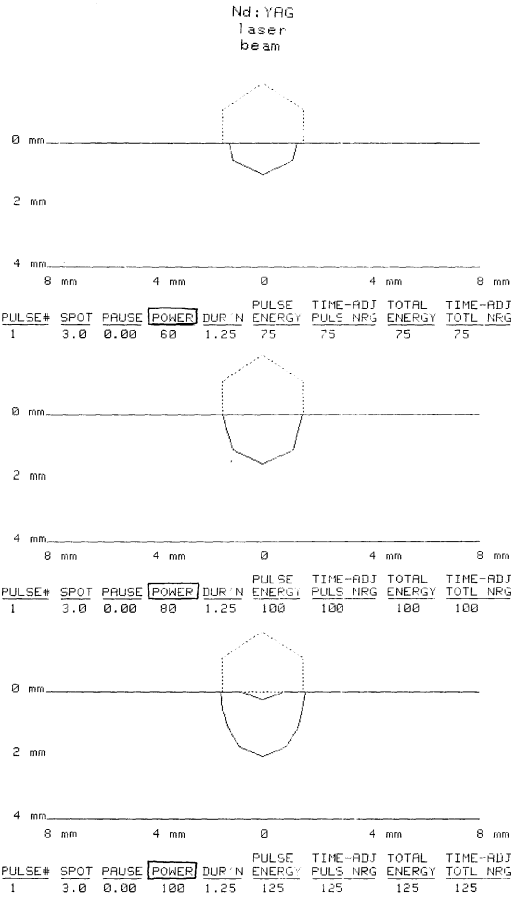


Figure 8. Changing power

cooling phase continues until the tissue reaches its baseline temperature. The cooling process has been referred to as the "heat sink effect" and is dependent upon such factors as blood flow and the physical characteristics of adjacent organs. Consider for example, delivering three one second pulses at a power setting of 80 watts to a 3 mm. area of tissue. The total energy delivered would be 3 x 1 x 80 or 240 watt-seconds. Imagine the effect of delivering this energy in two separate areas of the stomach. In the first area we apply each of the 3 pulses 30 seconds apart and in the other area we apply each of the 3 pulses 1/4 second apart. It is apparent that laser pulses separated by 30 seconds will provide little accumulative heating. The computer model quantitates this concept for us when it calculates the maximum

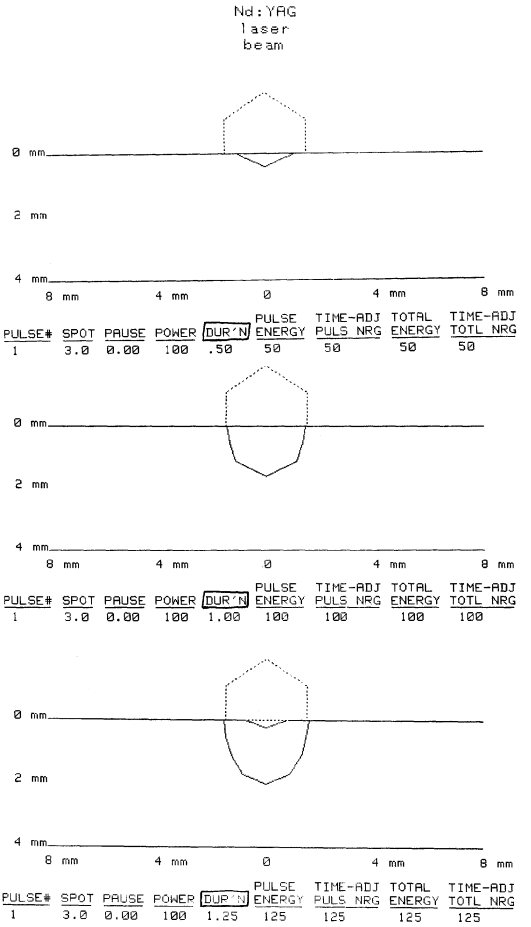


Figure 9. Changing pulse duration

temperature achieved within the two areas of irradiated tissue. In the first instance with a 30 second interpulse time interval a coagulated lesion is produced which measures 3 mm. in diameter and 2 mm. in depth. In the second case, using 30 second time intervals the coagulation lesion is approximately 50 percent larger and a crater is formed which is 2 mm. in diameter and 1 mm. deep.

TIME-ADJUSTED ENERGY

This observation points out the need for a new concept of pulse energy which takes into account heating from previous pulses. This concept requires the application of a correction factor to the pulse energy as measured by laser generator output. A rather

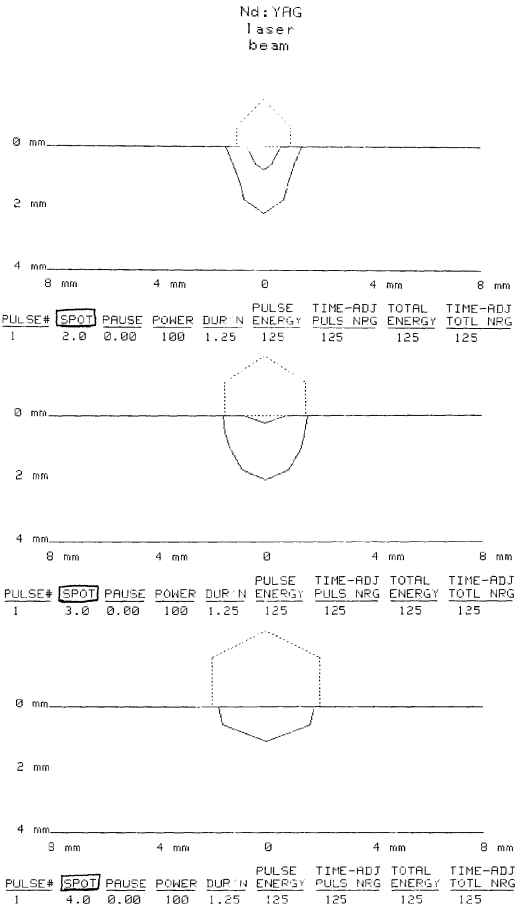
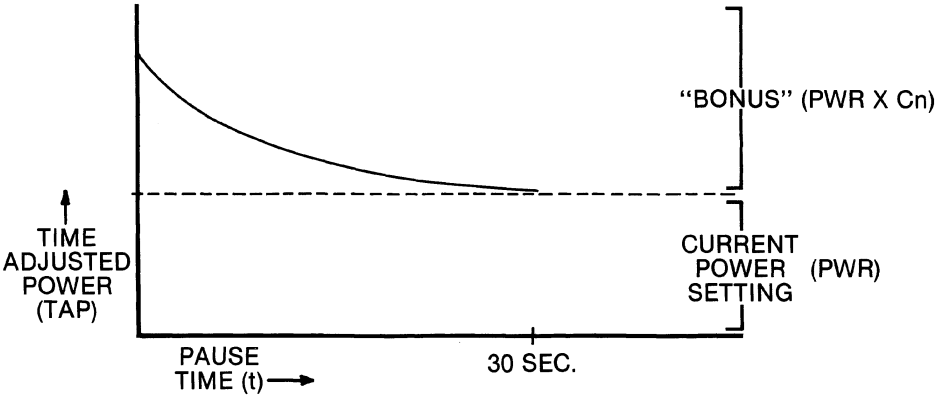


Figure 10. Changing spot size

simple first approximation of such a correction factor (here called "corrected energy" (Cn) factor) is represented in Figure 11. The basic concept involves developing a quantity called time-adjusted energy. This amounts to the actual energy delivered plus a "bonus". This bonus is maximal with an interpulse time interval of zero and is minimal at approximately the thermal relaxation of the tissue. The bonus is calculated by multiplying the power setting by our "corrected energy" factor. The Cn factor has two components. The first component represents a linear relationship with the ratio of the power setting of the previous pulse related to the maximum power output of the laser generator. This component sets the maximum for the bonus which would correspond to an interpulse time interval of zero. The second component

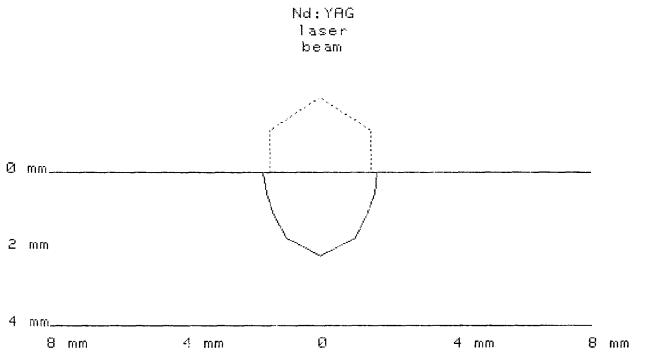


$$TAP = PWR + (PWR \times Cn)$$
$$TAN = TAP \times DUR$$
$$Cn = \left(\frac{PWR_{P-1}}{PWR_{MAX}}\right)\left(e^{-1/T_R}\right)$$

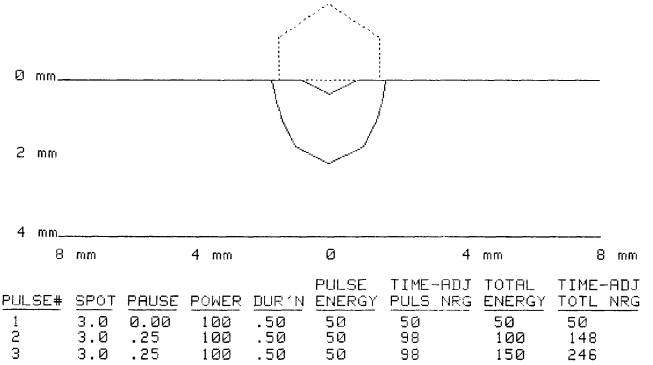
Figure 11. "Time-Adjusted energy"

of the Cn factor provides for the exponential decay of our energy bonus over time and is based upon the interpulse time interval expressed as a fraction of the thermal relaxation time of the tissue. In Figure 9 the maximum output of the laser generator is 100 watts and the thermal relaxation time is approximately 38 seconds.

Thus we have developed a "time-adjusted total energy" as opposed to a simple statement of total energy as measured by the laser generator output. The latter does not take into account timing between laser pulses and therefore cannot anticipate variations in tissue effect with various treatment patterns. Figure 12 graphically demonstrates this concept wherein a total energy of 250 watt seconds are delivered with two different treat-



PULSE#	SPOT	PAUSE	POWER	DUR'N	PULSE ENERGY	TIME-ADJ PULS NRG	TOTAL ENERGY	TIME-ADJ TOTL NRG
1	3.0	0.00	100	.50	50	50	50	50
2	3.0	2.00	100	.50	50	86	100	136
3	3.0	2.00	100	.50	50	86	150	223



PULSE#	SPOT	PAUSE	POWER	DUR'N	PULSE ENERGY	TIME-ADJ PULS NRG	TOTAL ENERGY	TIME-ADJ TOTL NRG
1	3.0	0.00	100	.50	50	50	50	50
2	3.0	.25	100	.50	50	98	100	148
3	3.0	.25	100	.50	50	98	150	246

Figure 12. Time-adjusted energy related to tissue effect

ment patterns.

We can see that the technique using quarter second inter-pulse time intervals created a theoretical divot in the tissue surface whereas using two second pauses caused no excavation. Clearly the total energy as measured by machine output alone (here 150 joules in both cases) cannot distinguish between these two tissue effects. The time-adjusted energies of 223 and 246 anticipate variable tissue effects related to the difference in therapeutic technique.

Such time-adjusted total energy values could easily be calculated by the small computer which is already present in most laser generators. These values would provide the clinician with a slightly more realistic measure of tissue effect. This

measure must be further mentally adjusted by the therapist using his general knowledge of average spot size and spacial distribution of the laser pulses within the treatment zone.

TISSUE EFFECTS

Laser radiation has several effects on tissue which lead to hemostasis, which is the hallmark of endoscopic laser therapy for gastrointestinal bleeding. Hemostasis is the therapeutic goal when treating bleeding. It is also the process of hemostasis which provides for the bloodless aspect of laser surgery when tissue ablation or inscision is the therapeutic goal.

Perhaps the most obvious tissue effect leading to hemostasis is simply the coagulation or congealing of blood as it flows in the blood vessels. This process presumably plays a major role in the smaller blood vessels and capillaries. The larger vessels usually require additional effects which provide for narrowing of their lumen and slowing of blood flow. Two such processes are tissue edema and thermal vasoconstriction. Edema results from changes in vascular permeability and becomes quite pronounced in laser irradiated tissue. It has a tourniquet effect on the blood vessels and perhaps a tissue sparing effect by decreasing the absorption coefficient of the perivascular tissue. This is achieved by effectively diluting the tissue constituents with water which tends to absorb less laser light. The blood vessel and its contents would theoretically be less affected by edema. Thermal vasoconstriction occurs when the vessel wall is heated to 80 degrees centigrade at which time the intramural collagen undergoes coagulative contraction. Such dynamic denaturation of interstitial collagen is visually evidenced to the laser therapist when puckering of the tissue occurs during irradiation. An additional hemostatic effect of laser light is thermal damage to the vascular endothelium. As this occurs procoagulation factors are released which result in the formation of a blood clot which then grows to occlude the lumen and provide lasting hemostasis. Table 2 summarizes the tissue effects of laser light.

CRITICAL TEMPERATURE	HISTOLOGICAL EVENT	ENDOSCOPIC MANIFESTATION
45°C	cell death, edema, endothelial damage, vasodilation	erythema, edema cuff
60°	protein coagulates	tissue turns grey-brown, blood turns black
80°	denatured collagen contracts, blood vessels constrict	tissue "puckers"
100°	tissue water boils	vaporization causes 4 divot
210°	dehydrated tissue burns	blackened tissue disappears ± glowing embers

Table 2. Critical temperatures

SUMMARY

Laser light is usually of a single wavelength and its radiation is harmoniously "in tune". This monochromatic and coherent nature of laser radiation provides a powerful tool for heating biological tissues in a very precise manner. The major photoabsorptive components of human tissue are water and hemoglobi each of which has its own characteristic absorption profile.

The fundamental event of photon tissue interaction is either absorption or scattering. These phenomena are mutually inter-dependent and determine the pattern of light intensities at all points within the tissue. Wavelength, tissue constituents and therapeutic spot size are major determinants of this intensity

pattern. The heating phase of laser tissue interaction follows a pattern established by the absorption-scattering phase and is further dependent upon power setting and pulse duration. The cooling phase of laser therapy begins with initial heating and continues until the tissue returns to its baseline temperature. This process is dependent upon the intrinsic thermal diffusivity of the tissue as well as the pattern of blood flow within the tissue. This process becomes a critical determinant when considering the effects of variable interpulse time intervals. A concept of "time-adjusted energy" has been developed to relate this aspect of therapeutic technique to tissue effect.

As tissue is heated, critical temperatures are reached for endothelial damage, cell death, protein denaturation, blood vessel constriction and tissue vaporization. These effects translate into various therapeutic goals, all of which share the hallmark characteristic of laser therapy . . . hemostasis.

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3. NATURAL HISTORY OF UPPER GASTROINTESTINAL BLEEDING AND DETERMINANTS OF OUTCOME

J. Johnston

Prior to a discussion of endoscopic hemostatic therapy, an overview of the spectrum of upper gastrointestinal (UGI) hemorrhage is appropriate with emphasis on its natural history and the various factors affecting its outcome. UGI bleeding remains a common and serious problem. It is estimated there are 100,000 admissions each year in the United States due to UGI bleeding from peptic ulcer disease alone (1). Overall, the mortality rate for UGI bleeding is approximately 8% to 10% (2-4). For those patients who continue to bleed after hospital admission or rebleed while in the hospital, the mortality rate increases to 20% (2,3,5). If urgent surgery is required for uncontrolled bleeding, the mortality increases further to approximately 25% (2-5). In contrast, if bleeding is controlled and then elective surgery is performed, the expected mortality rate falls to less than 3% (6,7).

The advent of routine fiberoptic panendoscopy during the last decade has enabled rapid and accurate diagnosis of the bleeding lesion in most cases (8). However, this improved diagnostic accuracy alone has not lowered the mortality rate, the need for surgery, or even the transfusion requirement (9,10). With the development of effective endoscopic modalities for hemostasis, an improved outcome might be anticipated in high risk patients with active bleeding at endoscopy or a high chance of rebleeding. Using safe and effective endoscopic hemostatic techniques in such cases, high risk, urgent surgery might be avoided, or replaced by a lower risk elective procedure.

The majority of the patients stop bleeding before they ever see a doctor and do not rebleed. Such patients would derive no benefit from an endoscopic therapy for hemostasis, and might be harmed. Therapeutic efforts need to be directed to those patients who continue to bleed, or are likely to rebleed. Table 1 lists some selected statistics about the natural history of UGI bleeding. Bleeding stops by the time of the admission or endoscopy in approximately 80% of cases (2-4). The incidence of active bleeding found at early endoscopy is greater than at endoscopy delayed for more than 48 hours (11). Although there are marked variations in the reported incidence of further bleeding after hospitalization, an approximate incidence is 25% for both continued and recurrent bleeding (2-4). Urgent surgery is required in about 20% cases of UGI hemorrhage (2-5).

About half of the patients with UGI bleeding in most series are over age 60, and half have one or more associated significant medical problems (4). Approximately 11% of patients present to the hospital with hypotension. While 75% of patients are transfused only one or more units of blood, 12% will require 10 or more units.

The usual frequency of bleeding upper gastrointestinal lesions is listed in Table 2 (4). The reported incidence of bleeding gastritis varies widely and cannot be accurately stated. Overall, peptic ulcer disease accounts for about half of UGI hemorrhage cases. In controlled trials of peptic ulcer hemostasis (Table 3), the reported incidences of active oozing, spurting, or stigmata of recent hemorrhage (such as a raised visible vessel, flat central red or black spots within the ulcer base or an overlying clot) vary considerably (12-15). Regarding the nature of active bleeding, most investigators have documented more frequent oozing than arterial spurting from ulcer beds, whereas a minority report only arterial bleeding. In approximately 30% of cases, the ulcer bed was clean without stigmata of recent hemorrhage.

A large number of individual factors are predictive of adverse outcome for UGI bleeding (2-4). These factors may be

Table 1. Natural history of UGI bleeding

Bleeding stops by time of admission or endoscopy	80%	(50-85)
Further bleeding	25%	(20-38)
Continued		
Recurrent		
Urgent surgery	20%	(10-35)

Table 2. Final diagnosis for UGI bleeding

Peptic ulcer	50 - 55%	
Duodenal		26%
Gastric		24%
Stomal		2%
Varices	15 - 20%	
Gastritis	9 - 25%	
Mallory-Weiss tear	7%	
Esophagitis	6%	
Tumor	3%	
Other	6%	

grouped into three general categories: severity of hemorrhage, concomitant disease, and rebleeding potential (Table 4).

In contrast to self-limited hemorrhage, massive UGI bleeding is less amenable to medical management, more likely to require emergency surgery for hemostasis, and carries a higher mortality rate. Massive bleeding is suggested by hypotension, or by a transfusion requirement of one or more units of blood every eight hours. Schiller reported that a blood pressure exceeding 100 mm Hg on admission was associated with a mortality rate of 7%, compared with a mortality rate of 32% for an admission blood pressure of less

Table 3. Appearance of peptic ulcers at endoscopy for UGI hemorrhage

Arterial spurting	3-16%
Active oozing	0-40%
Visible vessel nonbleeding	9-45%
Other stigmata	10-41%
No stigmata	23-34%

Table 4. Adverse prognostic factors for UGI bleeding

I. Severity of hemorrhage, indicated by:

- Hypotension
- 1 unit transfusion every 8 hours
- Red blood per rectum or nasogastric tube
- Failure to clear blood with nasogastric lavage
- Continued bleeding after admission
- Active bleeding at endoscopy
- Need for surgery

II. Significant concomitant disease

- Systemic illness (cardiovascular pulmonary, renal, hepatic, CNS)
- Age 60
- Stress (sepsis, postoperative, burn, trauma)
- Medical or surgical complication

III. Increased rebleeding potential

- Visible vessel
- Esophageal varices
- Stress gastritis
- Gastric malignancy
- Gastric ulcer
- Giant duodenal ulcer

than 80 (2). The actual rate of transfusions required is more significant than the total number of units for the entire bleeding event. Also, massive hemorrhage is often suggested by hematochezia, the inability to clear the stomach of fresh blood with nasogastric lavage, or by active bleeding seen at endoscopy. In a survey by the American Society for Gastrointestinal Endoscopy, active bleeding at endoscopy was associated with a mortality rate of 16.1%, compared to mortality of 6.7% without active bleeding (4).

The presence of a significant medical problem greatly increases the mortality risk of UGI hemorrhage. Mortality increases even further when several systemic diseases occur with the hemorrhage (4). Age greater than 60 years is also linked with increased mortality. However, older age often accompanies associated disease, and age per se is probably less important as an independent variable. Stress factors as reflected by an intensive care unit setting, sepsis, postoperative state or trauma also affect outcome adversely. The association of UGI bleeding with a medical complication, such as pneumonia, thrombophlebitis, pulmonary embolism or congestive heart failure, or with a surgical complication such as abscess formation or an anastomotic leak, increases the mortality rate up to 43% (2). These patient factors are important even with mild gastrointestinal bleeding, but become even more ominous when bleeding is massive.

Category III of Table 4 lists anatomic lesions that rebleed frequently and thereby increase the likelihood of surgery or death. The importance of rebleeding was emphasized by Avery Jones, who reported that patients who rebled while hospitalized had a 22% mortality rate, compared to a 2% mortality without rebleeding (3). If lesions likely to rebleed and require surgery can be identified and effectively treated endoscopically before rebleeding, mortality for UGI hemorrhage might be reduced. Regardless of treatment, some lesions, such as stress gastritis, varices and malignancy, have a poor outcome because of the poor prognosis attending the underlying diseases. With other

lesions identified as the source of recent UGI hemorrhage, such as peptic ulcers with a visible vessel, gastric ulcers and giant duodenal ulcers, early surgery has conventionally been recommended. Peptic ulcer patients are often healthy and have an excellent prognosis if the acute bleeding can be controlled.

The visible vessel concept represents an area where endoscopic therapy may be very important. Descriptions of visible vessels and other stigmata of recent hemorrhage can be found in the older literature. Avery Jones in 1956 described an ulcer with "a projecting vessel" and "blood stained area in the slough" (3). Tanner in 1964 described a pulsating pseudoaneurysm in the base of an ulcer (16). More recently, Foster reported that ulcers with stigmata of hemorrhage rebled in 42%, compared to 3% for ulcers without stigmata (11). At endoscopy, Griffiths found a discrete visible vessel in 9% of his patients with UGI hemorrhage and reported that all of them had significant further hemorrhage (17). The best work describing the frequency of visible vessels and their rebleeding potential is from two recent argon laser controlled trials for UGI hemorrhage. Storey, et al. found visible vessels in 45% of peptic ulcer patients with recent hemorrhage (12). Although this is a higher incidence than previously noted, these investigators employed emergency endoscopy and rather meticulous washing techniques to remove overlying blood clots from the ulcer base. As noted in Table 5, peptic ulcers with bleeding or non-bleeding visible vessels had further significant bleeding in 56% of cases. In contrast, ulcers with minor stigmata, such as a central flat red spot or mild oozing, had further bleeding in only 8%, and ulcers with no stigmata had no further bleeding at all. Similarly, Vallon, et al. (13) reported that a visible vessel or active spurting often correlated with further significant bleeding and the need for surgery (Table 6). On the other hand, the endoscopic finding of a central spot or clean ulcer base implied a good prognosis. It is now believed that the raised red spot termed a "visible vessel",

Table 5. Outcome based on peptic ulcer endoscopic features (Storey 1981)

	n	Further bleeding	Surgery
Visible vessel	56	56%	50%
Other stigmata	21	8%	8%
No stigmata	40	0%	0%

Table 6. Outcome based on peptic ulcer endoscopic features (Vallon, 1981)

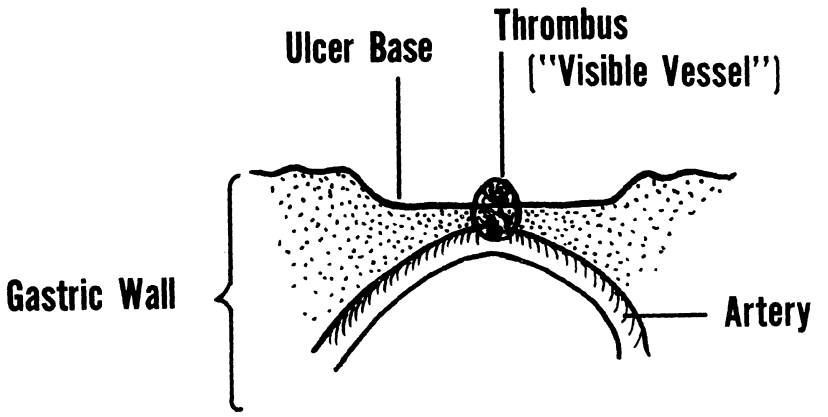
	n	Further bleeding	Surgery
Active spurting	13	85%	69%
Visible vessel	16	50%	31%
Central spot	39	10%	13%
No Stigmata	39	2%*	2%*

(*True bleeding lesion missed at endoscopy)

is usually not an exposed end vessel, but a thrombus emanating from a side hole in a deeper artery (Figure 1) (18; Bown, S., personal communication).

In conclusion, the various factors which are important in predicting the outcome of UGI bleeding have been outlined. Combinations of several factors (e.g. visible vessel with recent hypotension) may prove to be more important than individual factors alone. Certain factors, such as age and associated medical disease, will have an adverse effect on outcome regardless of the therapy for hemorrhage. In contrast, the poor outcome associated with other factors, such as a visible vessel, continued massive hemorrhage, or active bleeding at endoscopy, may be influenced by non-surgical treatment such as endoscopic hemostasis. The

Figure 1. Schematic diagram of a "visible vessel" in the base of a peptic ulcer.



natural history of UGI bleeding and prognostic factors are important considerations for planning or evaluating clinical trials of any hemostatic technique.

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4. ENDOSCOPIC CONTROL OF GASTROINTESTINAL BLEEDING WITH NON-LASER DEVICES

D. Jensen

Severe gastrointestinal bleeding is a significant clinical problem today. In spite of many improvements in medical and surgical care and blood banking, the hospital mortality remains between 8 and 10% in the United States (1-3). It has not changed in the last thirty years. Mortality from emergency surgery for bleeding ulcers is 15 to 27% in the United States compared with elective ulcer surgery in similar patients which carries a mortality ten times lower (2-8). Although 85 to 90% of non-cirrhotic patients with upper gastrointestinal bleeding have spontaneous hemostasis, patients with variceal bleeding and 10 to 15% of those with non-variceal upper GI bleeding often have more severe bleeding which requires intervention. Panendoscopy is the best way to diagnose the source of severe upper gastrointestinal bleeding. For 100 consecutive patients admitted for severe upper gastrointestinal bleeding at a large VA hospital in Los Angeles, the final diagnoses are shown in Table 1.

Peptic ulcers accounted for 52%, varices for 24%, hemangiomata for 10%, Mallory-Weiss for 8%, gastric eriosions for only 2%, tumors for 2%, and other lesions for 2%.

Some factors such as old age and the presence of other major medical problems exclusive of hemorrhage cannot be changed by medical or surgical therapy. Other factors such as continued bleeding despite multiple transfusions, active bleeding at endoscopy, the presence of a non-bleeding visible vessel often necessitate intervention such as emergency surgery. Their control by medical or endoscopic therapy without emergency surgery might improve survival after UGI hemorrhage.

In spite of the extensive use of emergency endoscopy for diagnosis over the last ten years, several studies failed to show any

Table 1. Final diagnosis of UGI bleeding site (% of total diagnosis)

Peptic ulcer			52%
Duodenal	24		
Gastric	16		
Pyloric	10		
Marginal	2		
Varices			24%
Esophageal	20		
Gastric	4		
Gastric angiomata			10%
Osler-Weber-Rendu		4	
Non-O-W-R		6	
Mallory-Weis tear			8%
Gastric erosions			2%
Duodenal erosions			2%
Tumors			2%
Other			2%

Table 2. Factors associated with increased mortality from UGI hemorrhage.

Age older than 60
Presence of another major medical problem exclusive of UGI hemorrhage
Persistent hypotension despite multiple transfusions
Transfusion of more than 6 units of blood
Active bleeding at endoscopy
A non-bleeding visible vessel
Malignancy or varices at endoscopy
Requirement for emergency surgery

consequent improvement in survival when compared to less aggressiv approaches to upper GI hemorrhage diagnosis such as elective endoscopy or routine UGI radiology (10-15). Emergency endoscopy for diagnosis alone has only allowed one to recommend earlier surgery. Now, however, different endoscopic methods of hemostasis offer specific treatment of bleeding lesions. Refer to Table 3.

Different methods for hemostasis are listed according to their mode of operation (thermally active, topical or injectable agents, and mechanical methods) and whether tissue contact is required wit endoscopic catheter or probe.

Argon (16) and neodymium-yttrium-aluminium garnet lasers (17) are used for endoscopic coagulation because these wavelengths can be efficiently transmitted through thin, flexible light guides,

Table 3. Endoscopic methods for hemostasis

	No tissue contact	Tissue contact
Thermally Active Methods	Laser photocoagulation Argon Neodymium-YAG Carbon dioxide Electrofulguration	Electrocoagulation Monopolar Bipolar Heater Probe
Topical or injectable agents	Clotting factors Tissue glues Ferromagnetic tamponade Collagen hemostat	Sclerotherapy Vasoactive drugs
Mechanical methods		Vessel clipping

which can be passed through the biopsy channel of panendoscopes. Coagulation by heating results when laser light strikes the tissue surface. The neodymium-yttrium-aluminum-garnet YAG wavelength penetrates tissue about four times deeper than argon. Electrofulguration results when a coabulating high-frequency electrical current arcs from an electrode tip to a tissue surface. Thermally active methods requiring tissue contact include electrocoagulation and heater probe. High-frequency electrical current in a coagulation waveform is used for electrocoagulation. There are bipolar and monopolar electrodes for endoscopic electrocoagulation (9). Endoscopic heater probes combine the effects of heat and pressure to seal bleeding vessels (18).

Noncontact topical agents are applied via an endoscopic catheter. Clotting factors (a mixture of cryoprecipitate and topical thrombin), tissue glues (for example, cyanoacrylate), and collagen hemostat adhere to vessels and thereby promote colagulation. In the ferromagnetic tamponade method (1), a mixture of tropical thrombin, vegetable oil, and iron powder is endoscopically directed via a catheter at the target and held in place by an external electromagnet.

Injectable agents are injected by an endoscopic needle into or near the bleeding lesion. Injection of sclerosing agents is being evaluated principally for hemostasis of esophageal varices (20). Endoscopic vessel clipping devices are not usually used to control

ulcer bleeding because of the difficulty in applying clips, especially in a field of blood.

The introduction of the "standard ulcer maker" by the University of Washington investigators (21) provided a reproducible method of creating uniform acute gastric ulcers. Such animal models have allowed investigators to quantitatively test the effectiveness and histologic damage of hemostatic devices and improve them if necessary before use in patients. Endoscopic topical hemostatic agents are easy to apply at a distance from the bleeding lesion via a catheter delivery system, are inexpensive, and are portable. No tissue damage has resulted from treatment of standard ulcers on a few patients. The major disadvantage is variable efficacy reported by different investigators. Unlike thermally active methods such as lasers or electrocoagulation, there is little convincing evidence that any topical agent can control active arterial bleeding or prevent rebleeding from arterial lesions. The hemostatic efficacy of various topical agents with standard ulcers has been reported by different investigators as 20% tot 90% (9). In a less severe, diffuse model of erosions and ulcerations induced by indomethacin, we reported that ferromagnetic tamponade was effective (19) but that clotting factors were not. There are few clinical data on efficacy of topical agents, which need further improvement and evaluation before clinical use is warranted.

Table 4 summerizes the results for thermally active endoscopic hemostatic techniques with bleeding canine standard ulcers.

Several investigators have reported promising clinical results for treatment of bleeding peptic ulcers or non-bleeding visible vessels in high risk patients using endoscopic monopolar electrocoagulation, argon laser, YAG laser, and bipolar electrocoagulation. However, most clinical series are neither randomized nor controlled.

More than 125 unselected patients with bleeding ulcers have been treated in uncontrolled series with monopolar electrocoagulation (23-28). Acute hemostatic efficacy was more than 90% and no complications were reported. Forty-four patients with bleeding ulcers treated with monopolar electrocoagulation (MPEC) were compared by Papp (23) retrospectively with surgical management of similar patients in his hospital. Patients treated with MPEC had shorter

Table 4. Efficacy and safety of thermally active endoscopic hemostatic methods in dogs.

Modality	Open studies*		Endoscopic methods	
	Efficacy**	Full damage***	Efficacy**	Full damage***
	%			
Laser				
Argon (8 to 10 W)	100	4- 8	93-100	10
Neodymium-yttrium-aluminium garnet (40 to 90 W)	90-100	77-97	100	43
Electrocoagulation				
Bipolar	80-100	0-30	97	17
Monopolar	90-100	3-50	100	53
Electrofulguration	90-100	0-20	-	-
Heater probe	100	0	93	13

* Done with stomach open at laparotomy.
** Percentage of complete stopping of bleeding from acute standard ulcers in heparinzied dogs.
*** Percentage of treated ulcers with full-thickness external muscle layer damage (9).

hospital stays (GU) or lower total hospital (GU and DU) than surgically managed patients. Contrasting these results, in a survey of German endoscopists using MPEC to treat 314 patients with UGI bleeding, the acute efficacy was 70% and 5 perforations were recognized (29). These results emphasize the variability and potential hazard of MPEC and suggest that technique is very important with this method.

We have extensively evaluated monopolar electrocoagulation in experimental ulcers (i, 30, 31) and clinically in several patients with ulcers and other bleeding lesions. A variety of probes (dry electrode, irrigator-coagulator electrode, hydrothermal probe, and hot biopsy forceps) with an analogue computer for energy quantitation have been tested. We were not able to standardize any of these devices for endoscopic use and their performance was extremely variable. Sticking was commonly a problem and the margin of safety was the lowest of any thermal device (30-32). Because of these problems we sought other devices for clinical trials.

J.M. Brunetaud (33) in France has reported the largest non-randomized consecutive series of bleeding ulcer patients treated with

endoscopic argon laser: 54 ulcers (32 gastric and 22 duodenal). He obtained immediate hemostasis in 85% but 11% rebled later. There were no complications. Failures occurred when bleeding vessels were not exposed before treatment (argon wavelength is absorbed by overlying blood), when large arteries like the gastroduodenal artery were massively bleeding, when ulcers were not accessible because of scarring or deformity, and when the power density was too low or high. During emergency endoscopy, Vallon et al. (34) randomly assigned ulcers with active bleeding, non-bleeding protruding vessels or localized red or black spots to argon laser treatment or control group. Active bleeding was controlled by argon laser in 10 of 15 patients (67%). However, there were no significant differences in outcome between argon laser or control groups for the parameters determined: rebleeding rate, operations or mortality in the bleeding or non-bleeding ulcer gourps.

Non-bleeding visible vessels in ulcers may be an indication for endoscopic hemostasis. Some investigators have reported rebleeding rates as high as 75 to 100% from untreated visible vessles within chronic ulcers (35-36). Using monopolar electrocoagulation, Papp treated nonbleeding visible vessels in benign ulcers. He randomized 26 patients either to control or treatment with monopolar electrocoagulation (27). Routine medical management of all patients include cimetidine and/or antacids. For the control group, there was a significantly higher rate of rebleeding (10 out of 13 patients or 77%), the hospital time was longer, and estimated cost higher than patients treated with monopolar electrocoagulation. Two patients in the control group died and none in the treatment group. The rebleeding rate in the treatment group was 7.7% (1/13 patients). Although there was not a statistical difference in mortality the difference in rebleeding rate was said to be statistically significant. Papp reported no complications of aggravation of bleeding with monopolar electrocoagulation.

Since initiation of our laser clinical trials, several portable, inexpensive, safe and effective thermal devices have been introduced, including heater probe and bipolar electrocoagulation. These warrant evaluation in controlled clinical trials. Heater probe and multipolar probe (a form of bipolar electrocoagulation) were both developed by the University of Washington investigators (21, 37).

Target irrigation and coagulation are possible with these probes. Both methods have probes which coagulate well with either the tip or sides of the probe and as effectively with tangential application as en face. Good efficacy in nonrandomized series has been reported for both bipolar electrocoagulation (BICAP) and heater probe. Small (~2.3 mm) and large (~3.2 mm) diameter probes have been tested. In our own experience 12 patients with active arterial ulcer bleeding and 22 patients with non-bleeding visible vessels and other non-ulcer bleeding lesions were treated with heater probe or bipolar electrocoagulation (38). The larger probes were more effective for bleeding control (84%) than smaller probes (66%). Compared with the smaller probes, larger probes coagulated better, washed more effectively, and required fewer applications for control of active bleeding. Recently, a multicenter pilot study with the small multipolar (BICAP) probe was reported for five centers in the United States and Europe (39). The efficacy for control of ulcer bleeding was 85% and there was a 24% incidence of rebleeding.

Important considerations for the choice of endoscopic hemostatic methods for clinical trials are outlined in Table 5.

Bleeding esophageal varices are effectively treated with endoscopic hemostasis. The realization that shunt surgery has not

Table 5. Comparison of endoscopic lasers, electrocoagulation, heater probe.

	Lasers	Electro-coagulation	Heater probe
Effectiveness	Excellent	Good	Good
Standardization	Excellent	Fair	Good
Ease of endoscopic use	Easy	More difficult	More difficult
Safety			
Perforation rate	Argon: none YAG: 1-2%	Bipolar: none Monopolar: <5%	None
Endoscopist hazard	Retinal damage	Electric shock	None
Cost (Initial)	More expensive	Less expensive	Less expensive
Catheter-probe	More expensive	Less expensive	More expensive
Portability	No	Yes	Yes
Use of standard hospital Utilities-outlets	No	Yes	Yes
Multipurpose use in large Hospital	Yes	No	No

improved survival for patients with portal hypertension and bleedin varices, endoscopic sclerotherapy is being resurrected as another choice. Also YAG laser has been used to treat bleeding esophageal and gastric varices. Keifhaber reported the largest unslected non-randomized series (40) with 142 of 155 treatments controlled active bleeding for efficacy acutely of 92%. Rebleeding was seen in 33 patients or 30%. Perforation occurred in one patient. Keifhaber recommended treating active variceal bleeding with YAG laser and then performing shunt surgery, because of the high rebleeding rates. Routine intensive care unit management, blood replacement, and correction of coagulation was also recommended. Using this approach, Keifhaber's overall mortality for Child's class A and B patients was 40% (23% for A and 55% for B). However, all of the Child's class C patients died. Other investigators prefer sclero-therapy for control of variceal hemorrhage instead of YAG laser and/or shunt surgery. MacDougall et al. recently reported signifi-cantly increased long-term survival in variceal hemorrhage in a controlled, randomized series using endoscopic injection sclero-therapy (41). 107 patients with cirrhosis and variceal hemorrhage were randomized either to repeated endoscopic sclerosis or control group. There was a statistically lower frequency of recurrent vari-ceal hemorrhages among the sclerosis group (43%-22/51-during treat-ment obliteration). For the control froup there was a 75% incidence (42/56 patients) of recurrent variceal hemorrhage. The overall risk of bleeding per patient month of follow-up was reduced threefold in the sclerotherapy group. By cumulative life analysis tables, the survival was shown to be significantly improved in the sclerotherapy group compared with the control group. Routine management consisted of blood transfusions and vasopressin; a Sengstaken-Blakemore tube was used if bleeding did not stop spontaneously. They used a flexib panendoscope with a flexible esophageal sheath. Injections of ethanolamine were begun as soon as the variceal bleeding was con-trolled and were repeated every three weeks until the varices were obliterated. In the 240 courses of injections, 21 patients had complications. The worst complication was esophageal perforation in 2 patients. One of the patients died. This patient had been endo-scoped with a rigid instrument. 15 patients had esophageal ulcers and 3 of these were the site of subsequent bleeding. Esophageal

strictures resulted in 9 patients and 4 of these required dilatations. The mean number of injection courses required for obliteration of esophageal varices was 4 with a range of 3 to 12. Other controlled trials of variceal sclerotherapy have been started. There are some preliminary reports that sclerosis of varices in patients who have never bled (prophylactic sclerosis) may be effective in reducing the incidence of hemorrhage. However, it is known that approximately 2/3 of patients with varices never have trouble with gastrointestinal bleeding whereas approximately 1/3 do. For treatment of active bleeding of esophageal varices, sclerotherapy also has been used. No large randomized controlled study has been reported which documents effectiveness of sclerotherapy for actively bleeding varices although several investigators have reported good efficacy in non-randomized studies (20, 42, 43).

Different results and conclusions in these clinical trials may be accounted for by differences in: a) technical skill and experience of investigators, b) patient and lesion selection, c) control groups chosen (retrospective versus prospective) and method of comparison, and d) parameters selected for comparison. Randomized controlled trials by skilled endoscopists after standardization of equipment and techniques are needed to assess the true effectiveness and safety of promising endoscopic hemostatic methods.

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5. ENDOSCOPIC AND PHARMACOLOGIC THERAPY OF UPPER GASTROINTESTINAL BLEEDING'. LASER VS. PHARMACO-THERAPY VS. AUTACID

P. Bright-Asare

Upper gastrointestinal bleeding remains a major clinical problem in medicine with an estimated hospital admission rate of 50-150 per 100,000 population for actue upper gastrointestinal bleeding (1,2). In 1983 it is a sobering fact that there is not always an effective therapeutic modality for upper gastrointestinal bleeding. The treatment is still fraught with futility. The mortality has remained between 10-15% for 40 years, despite advances in resuscitation and in the care of critically ill patients in intensive care units; and despite the ready availability of fiberoptic endoscopy, a modality which many thought would improve treatment and prognosis by early specific diagnosis. Finally, with the advent of effective anti-secretory histamine H_2 receptor antagonists it has been hoped that there would be a significant reduction in morbidity and mortality in upper gastrointestinal bleeding. However, neither cimetidine or other currently available antisecretory drugs effectively control upper gastrointestinal bleeding. (23) The principles in management of upper gastrointestinal bleeding should continue to be a team approach, covering:

1. Resuscitation
2. Specific diagnosis (endoscopy, radionuclide Tc^{99}, angiography)
3. Specific effective therapy.

1. RESUSCITATION

Over the past 30 years there have been impressive developments in the care of critically ill patients. This has not reduced the 10 to 15% mortality of patients with upper gastrointestional bleeding and there are several possible explanation for this unchanged high level

mortality rate. The bleeding patients that we now treat are much older and generally have more severe, sometimes multi-system underlying illnesses. (3, 5) Thus, these patients withstand bleeding poorly. Previous studies have demonstrated a close correlation between severity of bleeding and underlying medical condition. The effect of upper gastrointestinal bleeding may be devastating on the 70 year old patient with congestive heart failure, renal insufficiency, and cerebral vascular disease; similarly the young immunosuppressed patient may exsanguinate during resuscitative efforts. However, the 30 year old patient with no underlying medical illness often requires minimal specific intensive therapy for upper gastrointestinal bleeding.

Resuscitation remains the sine qua non for the care of the critically ill bleeding patient. The major steps in resuscitation shoul be well coordinated and synchronized in all institutions as a team effort involving the nursing staff in the emergency room, emergency room phisicians or house staff, internists gastroenterologists, surgeons, and radiologists, as well as other supportive staff in the care of patients. (3, 4)

Resuscitation should continue from the moment the patient is diagnosed as having upper gastrointestinal bleeding to the point he or she is stabilized and becomes ready for endoscopic and pharmacologic therapy, angiographic treatment, or surgery. That resuscitati is critical to the survival of patients is undoubted, however, the true benefits of the diagnostic or supportive components of resuscitation are not known. For example the value of routine electrocardiography in identifying underlying cardiac disease in patients over 35 years who bleed and the effect of this test on their survival is unknown.

Hemostatic benefits of ice/cold saline or water vs saline at roc temperature are not known. In any case despite sophisticated advances in critical care units for the management of patients with upper gastrointestinal bleeding there have been no changes in the mortality rate.

2. SPECIFIC DIAGNOSIS

With the ready availability of flexible fiberoptic instruments it has become possible for an endoscopist to correctly diagnose the source of gastrointestinal bleeding in 85-90% of patients. (6, 7, 8) However, the feeling of unbearable futility and impotence of the endoscopist able to visualize the source of the patients bleeding, but unable to arrest the bleeding has become a source of unexpressed deep despair. It has, therefore, become necessary to develop endoscopic methods that would control bleeding from the upper gastrointestinal tract.

3. TREATMENT

I. Endoscopic methods

The aims for endoscopic therapy for upper gastrointestinal bleeding are:

A) To prevent the need for urgent surgery.
B) To prevent rebleeding.
C) To temporize ("BUY TIME") while the patient's condition optimizes to undergo necessary surgery.
D) To enable intrinsic hemostatic mechanisms or pharmacotherapy to work.

The endoscopic therapy for upper gastrointestinal bleeding should consist of:

A) Continue stabilization of patient after resuscitation instituted and specific diagnosis is made.
B) To work conjointly with general measures and specific drugs such as PGE_2, cimetidine, ranitidine, sucralfate, etc. to achieve effective lasting hemostasis.
C) Both endoscopic (laser and electrocautery) and pharmacologic agents have to be individualized i.e. what works for duodenal ulcer with spurting vessel (laser) will not work for hemorrhagic gastritis (PGE_2).

In this chapter, we shall deal only briefly with the specific endoscopic modalities to control upper gastrointestinal bleeding. These have been dealt with adequately elsewhere; instead, this chapter will place endoscopic therapy for upper gastrointestinal bleeding in the perspective with currently employed pharmacotherapy for the control of upper gastrointestinal bleeding.

1) Laser is a non-contact method whereby a laser beam is directed at the bleeding lesion and the energy produced coagulates the tissue and stops the bleeding.
2) Contact methods utilize an endoscopic probe which directly touches the tissue and by producing thermal energy generated by the electrosurgical current, the heat coagulates the tissue and stops the bleeding.
3) The third method employs, by means of non-contact, a direct spraying of procoagulants at the bleeding lesion to stop hemorrhage.

II. Pharmacologic therapy

There is currently no effective pharmacological agent for the control of upper gastrointestinal bleeding (Figure 1 and 2). Cimetidine (15, 16) which is so widely and sometimes excessively prescribed for upper gastrointestinal bleeding is no better than placebo, and was especially not helpful in the treatment of gastric

Figure 1.

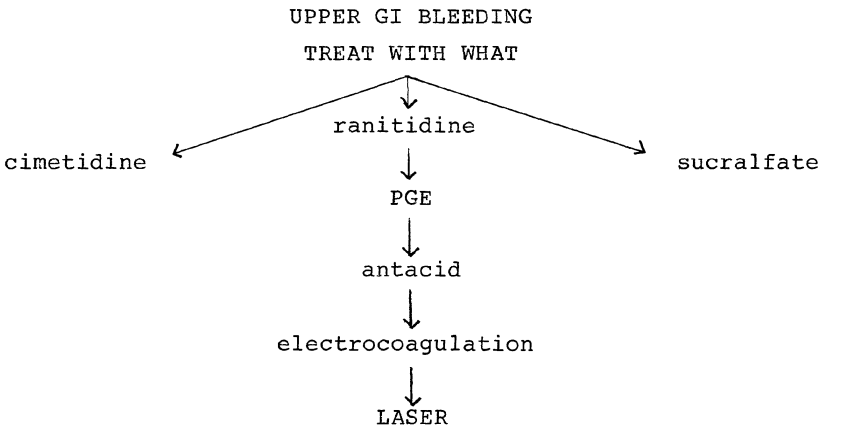
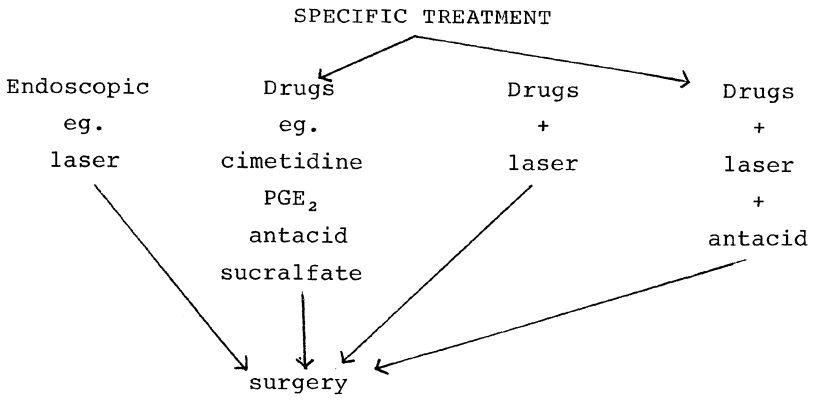


Figure 2.

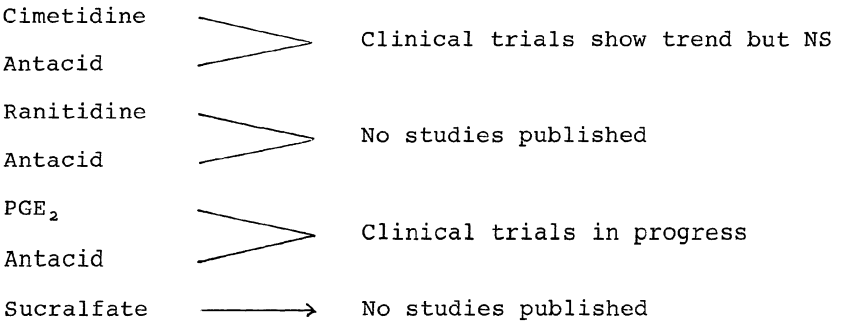


mucosal lesions. Although the role of cimetidine or ranitidine in controlling upper gastrointestinal bleeding from hypersecretory states such as peptic ulcer disease with high acid output or Zollinger-Ellison Syndrome has not been studied, it is reasonable to assume that they may be beneficial in these conditions. The treatment of uncomplicated gastric ulcer remains an enigma. Thus, it is not surprising to find that the pharmacologic therapy of a bleeding benign gastric ulcer remains frustrating and completely unresolved (Figure 3 and 4).

Figure 3. Upper GI bleeding.

For active bleeding	To prevent rebleeding
Cimetidine (C) no proven vlaue	Cimetidine + antacid appeared to work
Upper GI bleeding failed to stop in 25% of (C) treated patients compared with 17% of placebo patients gastric lesion especially failed to respond	Cimetidine + antacid may be beneficial in duodenal and peptic lesions
	Cimetidine not panacea for all upper GI bleeding Use has to be selective
	Same conclusion may apply to ranitidine

Figure 4.



Acute stress erosions and stress ulcers of the upper gastrointestina tract commonly occur in critically ill patients (9, 10, 11). In intensive care units such patients often have sepsis as a common denominator in the majority of cases (9, 10). Other risk factors include hemorrhage shock, severe trauma, head injury, renal or respirative failure, hepatic failure, and extensive burns. The pathogenesis although poorly understood have been postulated to include (13):

1) Broken gastric mucosal barrier with diffusion of hydrogen ions.
2) A decrease in mucosal blood flow with disturbances in mucosal microcirculation with vascular changes (9, 11).
3) Acute energy deprivation of mucosal cells with profound decreases in ATP levels (12).
4) Abnormalities in the utilization of ATP (12).
5) A change in chemical composition of gastric mucus.
6) Reflux of bile and lysolecithin with devastating effects on gastric mucosal membrane.

The amount of total gastric acid required for the genesis of erosion is not much. The mortality of surgical therapy for acute hemorrhagic gastritis is between 30-50% (11). While hemorrhage gastritis may respond variably to supportive measures, such as fluid replacement, treatment of sepsis, correction of coagulopathy, and intensive medication (mega-antacid therapy, antisecretory therapies, cimetidine, ranitidine, etc.), none of these modalities have shown consistent benefits in gastrointestinal bleeding in critically ill patients.

Vigorous antacid therapy to maintain the gastric pH above 3.5 to 4.0 is more effective than cimetidine (16) in preventing acute upper gastrointestinal bleeding (14, 15). Selective arterial infusion of pitressin may control bleeding (17, 18), but its side effects and inconsistent benefits may sometimes make it unacceptable. Anticholinergics, carbenoxolone, and multivitamins have a questionable effect.

Prostaglandins (Figure 5) of the A,E,F_{2R}, and I, series as well as their analogs have been shown to prevent gastric mucosal lesions produced by noxious agents or drugs (19-33). Ethanol, bile salts, strong acids, alkali, and chemotherapy in animals (42) and humans (34-41). Some of these prostaglandins inhibit gastric acid secretion, but others such as PGE_{2B} which protect the gastro-duodenal mucosa without inhibiting gastric acid secretion may do so by mechanisms generally termed cytoprotection that are poorly understood (20). Some of the proposed hypotheses to explain cytoprotection include (a) stimulation of gastric and duodenal mucus and bicarbonate secretion (26), (b) increase in gastric in gastric mucosal blood flow, and (c) stabilization of the membrane of gastric and duodenal mucosa to reinforce the "gastric mucosal barrier" (24, 33-35).

Figure 5.

PROSTAGLANDINS
Theoretically beneficial to gastric and duodenal mucosal structure and function

Antisecretory PGE
Cytoprotective PGE
> shown

experimentally to <u>prevent</u> gastroduodenal mucosal injury due to HCl, NaOH, bile, absolute ethanol, etc.

Clinical trials with PGE show increased rate of ulcer healing.
Six of 6 cases of severe hemorrhage gastritis treated with 15 R 15 methyl PGE_2 stopped bleeding.
Clinical trials for control of bleeding from gastroduodenal lesions with 15 R 15 methyl PGE_2 in progress.

Prostaglandins have also facilitated the rate of healing of both gastric and duodenal ulcers when compared to placebo.

In an open study 21 patients (unpublished data) with hemorrhage gastritis treated with oral 15 (R) 15 methly PGE_2 at different medical centers including our own (43) have stopped bleeding (27). In view of the dire consequences of bleeding from hemorrhage gastritis and the disappointing results of conventional therapy, these limited observations of 21 patients are encouraging. However, the true benefits of prostaglandins in the control of bleeding from hemorrhagic gastritis should be settled by the results of the multi-center double blind controlled trial which is currently in progress, in which our center is participating.

Cimetidine has no proven value in the treatment of upper gastrointestinal bleeding (15, 16). The multi-center study, which is currently only in abstract form, reported that upper gastrointestinal bleeding failed to stop in 25% of cimetidine treated patients compared to 17% of placebo treated patients. Gastric lesions especially failed to respond. However, cimetidine and antacid used togethe appeared to work. Thus, cimetidine and antacid may be beneficial in duodenal and peptic acid related lesions. However, cimetidine should not be used as a panacea for all types of upper gastrointestinal bleeding (Figure 3).

The same conclusions generally applies to ranitidine, a new more potent H_2 receptor antagonist, five times more potent than cimetidine, without the reported antiandrogen effects of cimetidine and withoutthe effects on drug metabolism such as prolongation of the half life of theophylline derivatives, benzodiazepines, and coumadin anticoagulants, as well as propranolol. It is clear, therefore, that pharmacologic agents, endoscopic laser, and electrocautery have to be individualized for the control of upper gastrointestinal bleeding. What may work for duodenal ulcer with a spurting vessel will not necessarily work for hemorrhagic gastritis.

III. Endoscopic laser and pharmacologic and antacid therapy

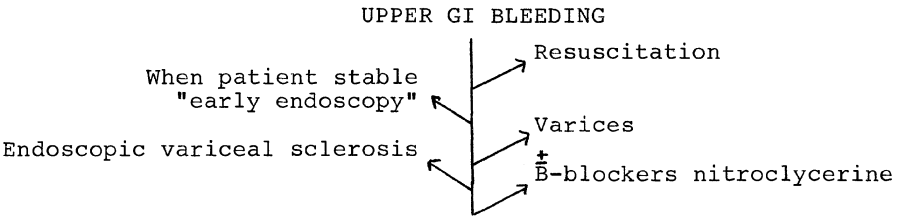
Endoscopic therapy will not necessarily affect the underlying pathophysiology of the gastric mucosal barrier, membrane stability, and mucus production that may characterize gastric and duodenal lesions that accompany sepsis or other stress situations. We propose

therefore a multidimensional approach to the management of upper gastrointestinal bleeding that utilizes endoscopic modalities and pharmacological therapy and antacid.

Illustrative cases

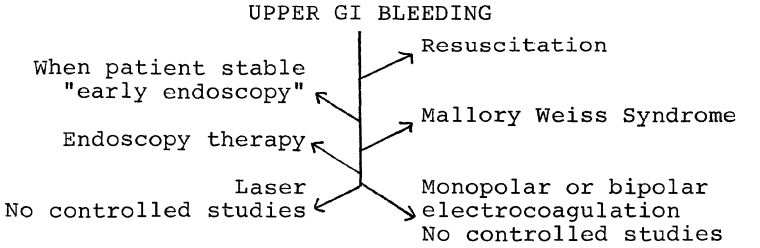
A 45 year old female with primary biliary cirrhosis presents with an upper gastrointestional bleeding. She is resucitated and when stable undergoes early endoscopy. She is found to have esophageal varices and may respond best to sclerosing of the varices, with the additional use of beta blockers or nitroglycerin without the use of laser or pharmacologic therapy (Figure 6).

Figure 6.



A 30 year old male chronic alcoholic is admitted with upper gastrointestinal bleeding. He is resuscitated, when stable after early endoscopy is found to have Mallory Weiss Syndrome. He may benefit from endoscopic therapy even though there are no controlled studies. Single case studies have shown benefit with monopolar and bipolar electrocoagulation. Thus urgent surgery may be prevented or postponed until the patient is well stabilized (Figure 7).

Figure 7.



Urgent surgery may be prevented or postponed in well stabilized patient(s).

A 45 year old patient with multiple trauma sustained in a holiday weekend motor vehicle accident is admitted with upper gastrointestinal bleeding. He is vigorously resuscitated, and when stable, diagnosis of hemorrhage gastritis without a spurting vessel is made at endoscopy. Such a patient may not benefit from laser. However, in view of the mucosal disturbances accompaning hemorrhage gastritis prostaglandins and high dose antacid should work.
The benefit of prostaglandins should be settled with the clinical trials that are in progress. Cimetidine, or ranitidine alone may not work in this situation (Figure 8).

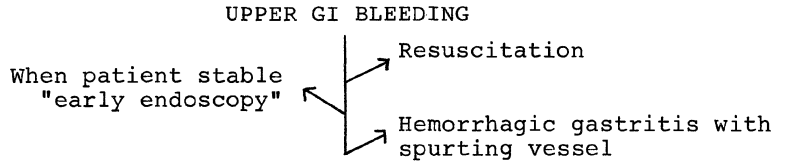
Figure 8.

UPPER GI BLEEDING

	Resuscitation
When patient stable "early endoscopy"	
	Hemorrhagic gastritis without spurting vessels
Laser minimal role	Cimetidine - antacid may work, not proven
PGE_2 - antacid should work, clinical trials in progress	Ranitidine - antacid may work, not proven

A 55 year old construction worker was sent from a major downtown construction accident with multiple head and bone injuries. He subsequently developed upper gastrointestinal bleeding. He is found at endoscopy to have hemorrhagic gastritis with a spurting vessel and would benefit from the use of laser or other endoscopic therapy for the initial control of the spurting vessels. But the concurrent use of pharmacologic angents namely, prostaglandins, PGE_2 or high dose, frequent antacids up to 120 ml per hour maybe beneficial. In this situation, cimetidine and antacids or ranitidine with high dose antacids may also work (Figure 9).

Figure 9.



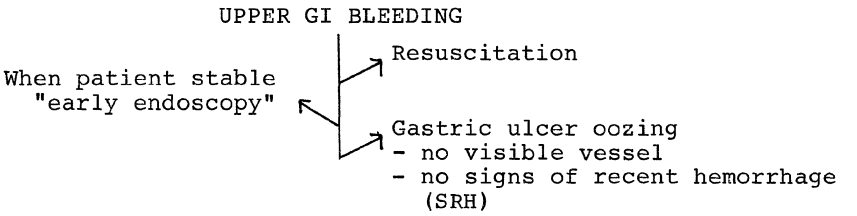
Laser for spurting vessel and drug therapy together

PGE_2 + antacid
should work clinical
trials in progress
Mega-acid 120/hr

Cimetidine + antacid
may work
Ranitidine + antacid
may work

A patient with upper gastrointestinal bleeding who is found to have a gastric ulcer oozing with no signs of recent hemorrhage, despite the absence of data from clinical trials, would be theoretically similar to the patient with hemorrhagic gastritis without a spurting vessle and should preferably receive prostaglandins or large dose frequent antacids (Figure 10).

Figure 10.

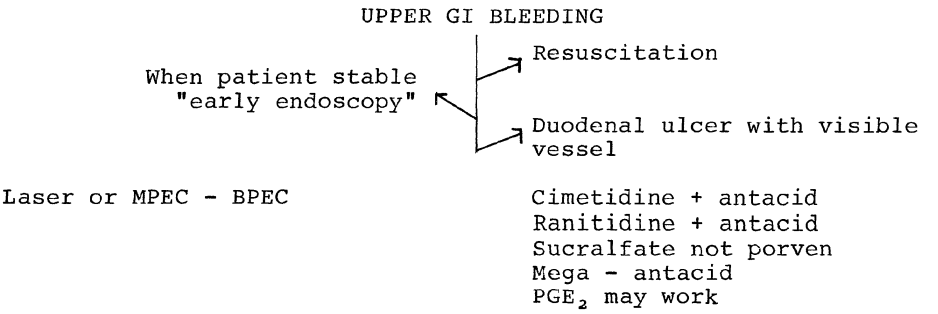


Try:
Laser in combination with drug
therapy
no data from clinical trials
Cimetidine + antacid may work

PGE_2 - antacid should work
clinical trials in progress
Ranitidine + antacid may work

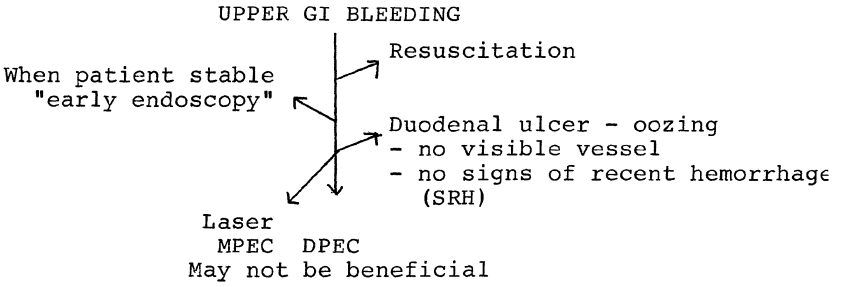
The patient with a duodenal ulcer with a visible vessel and signs of recent hemorrhage would benefit from endoscopic therapy to initially control bleeding from the visible vessel, with a concurrent use of antisecretory therapy namely cimetidine or ranitidine with antacid to control the underlying pathophysiology (Figure 11).

Figure 11.



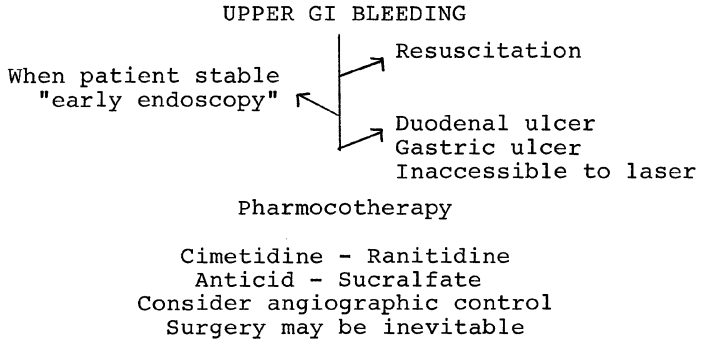
The patient with duodenal ulcer oozing with no visible vessel, no signs of recent hemorrhage may just benefit from drug therapy and effective antisecretory therapy antacid plus H_2 receptor antagonists (Figure 12).

Figure 12.



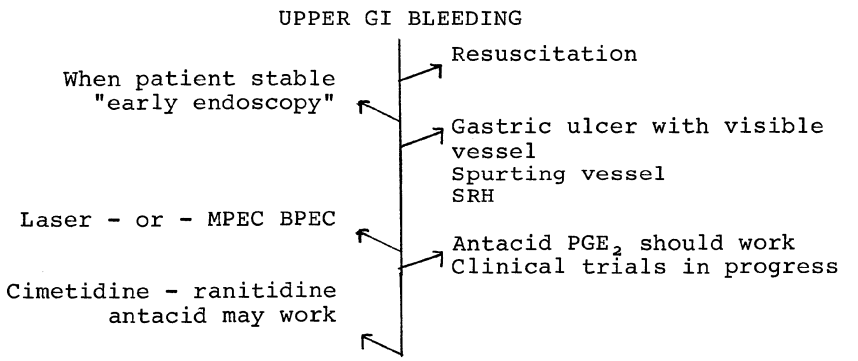
A 70 year old undernourished potbellied male patient is admitted with upper gastrointestional bleeding. He is vigorously resuscitated. When stable, endoscopy shows a gastric ulcer and a duodenal ulcer inaccessible to laser due to pyloric canal narrowing and duodenal bulb deformity. Angiographic control could be attempted. Surgery may be necessary for this patient once he is stabilized (Figure 13).

Figure 13.



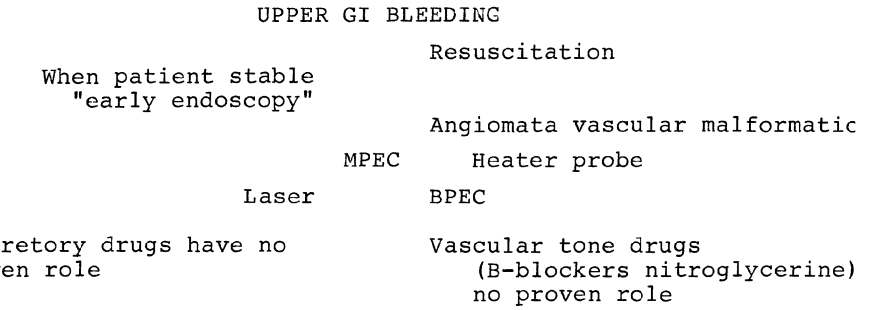
A 60 year old male patient presents with massive gastrointestinal bleeding. He is vigorously resucitated in the emergency room and when stabel undergoes early endoscopy, he is found to have a gastric ulcer with a visible vessel and signs of recent hemorrhage. Such a patient would clearly benefit from laser (or monopolar of bipolar electrocoagulation) for the initial control of bleeding. At the same time antacid and prostaglandins should work. Since cimetidine has not been found to be effective in the control of bleeding in such patients, cimetidine and ranitidine should be combined with antacid since these are the only agents currently available in North America and Europe (Figure 14).

Figure 14.



A 60 year old female patient presents with upper gastrointestinal bleeding; at endoscopy she is found to have vascular malformations. She would benefit from endoscopic therapy, namely laser or electrocoagulation. In such patients antisecretory drugs, H_2 receptor antagonists, prostaglandins, and drugs conferring cytoprotection have no proven value (Figure 15).

Figure 15.



CONCLUSION

Prostaglandins are not clinically available and are still investigational. The true benefits of prostaglandins should await the results of the multicenter clinical trials currently in progress. Cimetidine and raniticine are both clinical available in the United States, Europe and different parts of the world. Their benefits in upper gastrointestinal bleeding are, however, equivocal. High dose antacids should still be used. To date no form of endoscopic therap (either laser, electrocoagulation, thermal probe, or spray techniques) has been unequivocally established as causing a reduction in mortality. However, by the initial effectiveness of laser to control bleeding the physician may be able to temporarize sufficiently to stabilize these patients to more effectively continue resuscitation on stabilized patients and to enable surgery to be performed in a high risk group of patients. At the same time effective endoscopic therapy may enable pharmacological therapy to control the disordered homeostasis.

The pathophysiology of the underlying gastro-duodenal mucosa in the patient with severe hemorrhage gastritis is complex and often refractory to therapy. In such patients it must be stressed that the application of heat energy or laser energy to coagulate the tissue and stop bleeding does not necessarily affect the underlying processes such as loss of mucosal intergrity, disturbed gastric mucosal barrier, abnormal utilization of ATP and production of a poorly resilient mucus. Indeed, supportive measures such as adequate enteral or parenteral nutrition, treatment of underlying infection, and treatment of cardiac arrythmias may be crucial in stabilizing the patient and enhancing the response to treatment. These measures may help in correcting the underlying gastrointestinal disorder.

Therefore, laser and non-laser endoscopic therapy are only part of our armamentarium to control upper gastrointestinal bleeding.

A reduction in the mortality of upper gastrointestinal bleeding may only be seen when optimal pharmacological and supportive therapy are utilized along with endoscopic laser or non-laser therapy, when indicated, to either prevent need for urgent surgery, or prepare a critically ill patient to undergo difficult surgery in as elective a setting as possible.

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6. EUROPEAN EXPERIENCE WITH ND:YAG AND ARGON LASER FOR THERAPY OF UPPER GASTROINTESTINAL BLEEDING

P. Rutgeerts, K. Geboes and G. Vantrappen

On the pioneering work of Kiefhaber with the Neodymium-YAG laser and Frühmorgen with the Argon laser, both lasers are now being used for hemostasis of gastrointestinal bleeding in at least 50 European centers. More centers have employed the laser in the past but used it only for experimental work. The YAG laser is more widely used than the Argon laser because most investigators feel it has a higher hemostatic capacity. Despite its widespread applications, the clinical contribution of laser photocoagulation for upper gastrointestinal bleeding remains in some doubt. Evaluation of the uncontrolled data is difficult for several reasons. Firstly most upper gastrointestinal bleeding is self limited and abates without any therapeutic intervention. Secondly a lot of the uncontrolled data gives information only regarding initial hemostasis. A more important question is the effect of laser photocoagulation on the overall outcome in a particular patient. However the overall data of uncontrolled studies using lasers for the therapy of gastrointestinal bleeding present impressive results. In a 1979 survey (Figure I) initial hemostasis was achieved in approximately 90% of some 2,000 patients treated with both argon and Neodymium-YAG lasers in 37 centers in the world. Some of these investigators[1-13] have published subsequent data in more detail. The results of the controlled trials of laser therapy in the treatment of upper gastrointestinal hemorrhage will be the focus of the next chapter of this text.

ARGON - LASER

		Bleeding Lesion	Pts.	% Success
BRUNETAUD	France	87	80	87
WAITMAN	USA	50	20	94
FRUHMORGEN	W. Germany	43	41	83
DWYER	USA	34	21	70
Le BODIC	France	18	14	82
LAURENCE	G. Britian	12	10	70
MANEGOLD	W. Germany	10	10	100
		254	196	

Nd-YAG - LASER

		Bleeding Lesion	Pts.	% Success
KIEFHABER	W. Germany	587	459	94
SCHONEKAS	W. Germany	334	298	93
DWYER	USA	106	71	87
POSL/SANDER	W. Germany	83	61	97
RHODE	W. Germany	83	61	92
RAMIREZ	Mexico		80	
WEINZIERL	W. Germany	77	70	74
GHEZZI	Italy	75	65	87
VANTRAPPEN	Belgium	53	50	96
WOTZKA/KAES	W. Germany	48	35	81
ULTSCH/BADER	W. Germany	37	27	88
STAUBER	Austria	30	28	80
FIEDLER/WALDM.	W. Germany	30	25	80
KREUTZER	Austria	29	25	90
RICHTER	W. Germany	25	20	92
ESCOURROU	France	22	20	75
IMMIG	W. Germany	22	14	82
KNOP/HAUSAMEN	W. Germany	22	20	82
MARCON	Canada	20	18	75
IHRE	Sweden	15	15	93
DIXON	USA	15	12	100
TROIDL	W. Germany	12	10	85
VIETS	W. Germany	11	11	100
BECKLY	G. Britian	11	9	82
CLASSEN/WURBS	W. Germany	10	10	100
ZIMMERMAN	W. Germany	5	5	100
SOEHENDRA	W. Germany	3	3	100
STADELMANN	W. Germany	3	3	100
TIJTGAT	Netherlands	3	3	75
DEYHLE	Switzerland	3	3	100
MOCKEL	W. Germany	3	2	100
		1776	1533	

The largest experience with the use of lasers for upper gastrointestinal bleeding is that of Kiefhaber, who reports a success rate of 94% hemostasis in the treatment of approximately 1,000 bleeding incidents in which he has used the Neodymium-YAG laser. In additional to successful hemostasis he claims to reduce the need for emergency surgery and he has also diminished the mortality rate. Surprisingly a high efficacy of laser therapy was reported for hemostasis of variceal bleeding[1,3,5]. The recurrence rate of bleeding however, was very high so that this modality cannot be considered as final. Most gastroenterologists do not use laser beam hemostasis in variceal bleeding or only for initial hemostasis and are treating the patients subsequently with sclerotherapy.

Besides the type of laser, other parameters are important for photocoagulation hemostasis, i.e. laser power and application time. These parameters often differ from one center to another. For the Neodymium-YAG laser, our studies[14-15] and also those of Bown et al.[16] have shown that short pulses of one second or less, and a power of 60-90 watts are most effective in the control of bleeding from experimental ulcers, causing less injury to the irradiated tissue. Consequently, in clinical medicine we used an unlimited number of such pulses for the treatment of severe bleeding. In contrast, Sander[2] used high power pulses for a duration of up to 10 seconds. Kiefhaber begins the treatment with short high power pulses, but increases the duration to control persistent bleeding. With Argon lasers most centers[17] used a power of 6 to 8 watts measured at the fiber tip and did not have any fixed maximum duration for laser exposure.

Stomach cleansing prior to therapeutic endoscopy is carried out in our department in all patients with hematemesis. In severely bleeding high risk patients, endoscopy is carried out with endo-tracheal intubation, but seldom with general anesthesia. Complications of laser therapy are not frequent in the reported series probably because this therapy has been applied very cautiously. Emergency endoscopy carries its own risk in actively bleeding and ill patients. The frequency of bronchopulmonary complications is underestimated. When aspiration of blood is suspected immediate careful bronchial cleansing has to be carried out. A perforation risk, reported to be 1-2% in the larger series, seems acceptable. Initial exacerbation of bleeding occurs at least in one out of five patients with spurters or non-bleeding vessels. Photocoagulation around the vessel before hitting the vessel itself would decrease this risk. Laser photocoagulation may contribute to complications simply by the inherent prolongation of the procedure or the use of a single channeled instrument blocked by the introduced fiber. Therefore we found the double channeled small caliber XGIF-2T instrument of Olympus, with a supplementary separate cleaning channel very suitable for operative laser endoscopy. Rapid gas distension of the stomach can be avoided. Additionally there is no problem reaching duodenal lesions. Increase of ulcer size occurs frequently after treatment, due to laser-induced ulcer transformation. In a few patients we noted a transient increase in serum

transaminases after laser treatment.

The main problem still remains the treatment of severe arterial bleeding. We and others are trying to improve the results of laser treatment in several ways. Improved endoscopic techniques should allow a better approach to all bleeding lesions. Repeated laser treatment for recurrent bleeding increases the efficacy but also the risk for perforation. According to Kiefhaber the risk should be minimal 48 hours after the first treatment. High flow CO_2 jet increases the success rate and reduces the total laser energy required for hemostasis, but causes distension problems. Elective surgery should have its place in the management of high risk patients after photocoagulation. Spurting or nonbleeding arterial vessels in the base of a deep ulcer are very difficult to treat by laser. Acute ulcers bear also a risk of perforation by laser therapy because of their shallow depth and the absence of fibrotic tissue at the ulcer base. Other lesions are difficult to treat because of their location: i,e. superior flexure of the duodenum, the fundic region and the upper part of the posterior wall of the stomach. In contrast, ulcers of the anterior wall and the greater curve, the angle, the antrum of the stomach and the arterior wall of the bulb are locations ideal for laser treatment.

Finally, laser machines are not yet optimally working. Information obtained by a questionnaire answered by 34 centers and collected by Rohde from Marburg[18] revealed that

75% of the doctors had encountered defects of the laser equipment: the light guide was responsible for 54%, the laser machine 32% and the laser endoscope for 14% of the defects. We have encountered damage of the optical bundle of the scope caused by laser photocoagulation on two occasions.

In the great majority of European centers lasers are used for the photocoagulation of gastrointestinal angiomas. This treatment seems very effective. In our department[19] we have treated 32 patients with angiomas. The best results were obtained in angiodysplasia of the colon while recurrence of bleeding was frequent in upper gastrointestinal angiomas or diffuse angiomatosis of the gastrointestinal tract. Recurrence of bleeding was mostly due to unrecognized lesions missed at endoscopy or to the formation of new lesions. Recurrence of bleeding from lesions treated by photocoagulation occurred rarely. We have treated a patient with a large bleeding haemangioma occupying the whole bulb. Near total disappearance of the lesion was obtained without rebleeding during or after therapy.

A new feature in laser research is the use of cytoprotective drugs to limit the damage caused by laser photocoagulation. We have recently shown[20] that laser induced stomach ulcers in dogs pretreated with 15(R)-15 Methyl Prostaglandin E_2 in cytoprotective doses heal much more quickly than ulcers in control dogs. Pretreatment, however, does not influence the acute coagulation effects of the YAG laser.

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7. CONTROLLED TRAILS OF LASER THERAPY IN THE TREATMENT OF UPPER GASTROINTESTINAL HAEMORRHAGE

S. Bown

Since the first endoscopic laser treatment in man in 1975 (1) there have been many anecdotal reports of successful treatment of hemorrhage from lesions of the upper gastrointestinal tract. However, gastrointestinal hemorrhage is often a self limiting condition and true assessment of the value of laser therapy can only come from controlled trials, the first of which was not reported until 1981.

Seventy to eighty per cent of upper gastrointestinal bleeds cease spontaenously (2). Any trial assensing the value of an endoscopic form of therapy must be able to identify the lesions most at risk of further hemorrhage if left untreated. Varices have a high risk. Little data exists for Mallory Weiss tears and the more diffuse lesions (oesophagitis, gastritis and duodenitis) but peptic ulcers are by far the most frequent lesions to go on bleeding (2) and most work has been directed towards endoscopic identification of the ulcers most at risk.

In 1978, Foster et al. (3) described 3 stigmata of recent hemorrhage (SRH) seen at endoscopy (a) fresh bleeding from the lesion; (b) fresh or altered blood clot or black slough adherent to the lesion; (c) a vessel protruding from the base or margin of the ulcer. Twenty-five of their 60 ulcers with SRH rebled (42%) compared with 1 of 29 (3%) without SRH ($p < 0.001$). In 1979, Griffith et al (4) reported that in 28 of 157 ulcers that had bled (18%) visible vessels were identified endoscopically and all these rebled (even though only 11 were seen to bleed at the initial endoscopy) compared with only 29 of the other 129 (22%). This was a retrospective study, and no comment was on how often the ulcer crater could be fully visualised or when blood clot obscured the ulcer

base. The first 2 Argon laser trials (5, 6) provided more precise data obtained in a prospective manner. We showed that when ulcers were washed endoscopically to clear overlying clot, visible vessels could be identified in 56 of 117 ulcers (48%) in which the crater could be fully examined. Nineteen of the 34 such cases not reated with the laser (56%) rebled compared with 1 of 13 ulcers with other SRH (8%) providing even stronger evidence that the visible vessel (whether bleeding or not at initial endoscopy) is a much more important prognostic indicator than any of the other stigma. However, even in this high risk group, only just over half rbled (7). In all these publications, the incidence of rebleeding in ulcers without SRH has been almost zero. All these reports are fully consistent with each other – the only idfference is the extent to which the ulcer crater was washed to identify visible vessels under overlying clot.

Identification of the presence or absence of a visible vessel is the main difference between the controlled trials to be described belwo. The early Nd YAG trials which did not do so, showed no benefit whereas the other trials stratified their cases with this in mind and have produced more encouraging results.

Results of trials

Eight controlled trials have been reported to date; 3 with the Argon and 5 with the Nd YAG laser. Four have only been published in abstract form, and so the details are limited but an attempt is made here to carry out a comparative analysis of the results for each laser:

ARGRON LASER

The 3 trials reported are Vallon et al. (1981)(5); Swain et al. (1981)(6); and Jensen et al. (1982)(8).

Vallon (5)

In this trial carried out in Barcelona, from an unselected series of 332 patients presenting with upper GI hemorrhage, 178 had peptic ulcers and all 136 with SRH were included in the trial. Randomisation to laser or sham therapy was carried out at the time

Table 1. Trial results — Vallon et al.

	LASER				CONTROL			
	Total	Rebleed	Surg.	Died	Total	Rebleed	Surg.	Died
Spurting	15	7	7	2(0*)	13	11	9	3(2*)
Visible vessel (not bleeding)	19	8	6	3(2*)	16	8	5	3(3*)
Red or black spots	34	5	2	0	39	4	4	4(0*)

* Post rebleed.
No significant benefit has been shown in any of these groups.

Table 2. Trial results — Swain et al.

	LASER				CONTROL			
	Total	Rebleed	Surg.	Died	Total	Rebleed	Surg.	Died
Spurting	7	4	4	-	4	4	2+≠	2(2*)
Visible vessel (not bleeding)	17	4	4	-	24	13	12≠	5(5*)
Oozing	2	-	-	-	4	-	-	-
Other SRH	5	1	1	-	6	-	-	-

* post rebleed.
+ 1 died before surgery: ≠ 1 treated with laser after rebleed out of trial.
Groups 1 and 2 combined - $p < 0.05$.
Group 2 alon - $p < 0.05$.

Table 3. Trial results — Jensen et al.

	Total	Rebleed	Surg.	Died
Laser	6	-	1 (elective)	-
Control	6	4	4 (all emergency)	1

of endoscopy with stratification in 3 groups — spurting arterial hemorrhage, non-bleeding visible vessels, and red or black spots in the ulcer base. Randomization was carried out whether or not the bleeding point was technically accessible. The results are shown in Table 1.

Swain (6)

In our trial, carried out in London, from an unselected series of 330 patients presenting with upper GI hemorrhage, 155 had pept. ulcers and 108 had SRH. Sixty-nine were finally considered to fulfill all the criteria for inclusion, the others being excluded on grounds of inadequate visualisation or access to the bleeding poir (22) or other external factors such as breakdown of the laser of unavailability of an experienced operator (17). Stratification was in 4 groups: spurting arterial hemorrhage, non-bleeding visible vessels, oozing, and stigma other than a visible vessel without active bleeding. Randomisation was carried out at the time of endc scopy. The results are shown in Table 2.

Jensen (8)

This controlled study is from Los Angeles. Twelve patients with spurting arterial hemorrhage were included and the results are shown in Table 3.

Thise 3 trials show a trend towards benefit in the treatment of spurting arterial hemorrhage and this reaches significance ($p < 0.0$ in the Vallon trial if 2 inaccessible duodenal ulcers are excluded in the laser treated group. The numbers in each trial are small, but combining all 3 and excluding inaccessible cases in the treate group of the Vallon trial, 9 of 26 treated spurting arteries had further hemorrhage compared with 18 of 23 controls ($p<0.005$). Comparison of the results for non-bleeding visible vessels is not quite so simple, as the Vallon trial included inaccessible lesions in their protruding vessel group. In addition, the lesions they described as red or black spots included cases in which a single spot resistant to washing was seen in the ulcer crater (Vallon; personal communication). Some of these might have been classified as visible vessels in our trial, and indeed the rebleeding rate in this group both treated and untreated was considerably higher than in our no visivle vessel groups. Our trial showed a benefit in thi group. Four of 17 treated and 13 of 24 controls rebled ($p < 0.05$).

In all 3 trials, all death associated with rebleeding were in cases with a visible vessel (there were some other deaths not assc ciated with rebleeding). Vallon reported 3 such deaths in treated patients and 5 in controls, we reported none and 7 and Jensen none

Table 4. Trial results — Ihre et al.

	Total	Rebleed	Emerg surg.	Died
Laser	12	5	5	2
Control	13	5	5	2

There was no significant difference between the 2 groups.

Table 5. Trial results — Rutgeerts et al.

	LASER				CONTROL			
	Total	Rebleed	Emerg surg.	Died	Total	Rebleed	Emerg surg.	Died
Group 1 (spurting)	23	14	14	7(7*)	NIL (ethical reasons)			
Group 2 (active bleeding)	38	2	1	6(1*)	32	12	4	5(4*)
Group 3 (non-bleeding)	14	3	2	2(2*)	22	7	5	3(2*)

* Post rebleed.
In Group 2, there was a significant benefit in the laser treated cases compared with controls ($p < 0.001$).

Table 6. Trial results — Swain et al.

	LASER				CONTROL			
	Total	Rebleed	Emerg surg.	Died	Total	Rebleed	Emerg surg.	Died
Group 1 (spurting)	6	2	2	1(1*)	6	5	4	1(1*)
Group 2 (visible vessels)	11	1	1	-	14	7	5	2(2*)
Group 3 (other SRH)	9	-	-	-	9	1	1	1(1*)

* Post rebleed.
There was a significant difference between the treated and control groups, both for the whole trial ($p < 0.02$) and for ulcers with a visivle vessel alone (p 0.02).

Table 7. Trial results — MacLeod et al.

	Total	Rebleed	Emerg surg.	Died
Laser	8	1	1	-
Control	8	8	8	2

There is a significant benefit in the treated group.

and 1 respectively. In total, 3 treated and 13 control patients died following a rebleed.

It is difficult to give a statistical value to this as the appropriate total number of patients is difficult to define, but the difference appears large. Vallon comments that they did not demonstrate a significant benefit for the laser and that more trials were necessary. However, looking at the results now available from 3 trials, a benefit appears to have been shown in both rebleeding rate and mortality.

Nd YAG LASER

The 5 trials discussed are Ihre et al. (1981)(9); Escourrou et al. (1981)(10); Rutgeerts et al. (1982)(11); Swain et al. (1982)(12) and MacLeod et al. (1982)(13).

Ihre (9)

This trial from Stockholm was limited to patients who had had a massive bleed (more than 3 units of blood required to restore the circulating blood volume) and who were actively bleeding at the time of initial endoscopy. Fourty-two patients fulfilled these criteria. Twenty-three were randomized to receive laser treatment, but in 8 cases this was technically impossible, 5 due to poor access and 3 due to other problems. Nineteen were randomized to th control group. Both ulcers and varices were included. For ulcers, the precise nature of the bleeding point was not discussed, and no comment made on whether a visible vessel was seen or was accessibl to therapy. The results for ulcers are shown in Table 4.

Escourrou (10)

This trial has been published as an abstract and was carried ou in France. Like the Swedish trial it was limited to patients with massive bleed who were actively bleeding at initial endoscopy. There was no discussion of how often the precise bleeding point could be identified within the ulcer crater nor whether this was a single vessel or diffuse oozing. Seventy-one ulcers were randomize and there was no difference in the mortality or need for emergency surgery between treated and control groups.

Rutgeerts (11)

This trial from Belgium is the largest so far reported with the Nd YAG laser. From an unselected series of 338 patients presenting with upper GI hemorrhage, 152 with stigmata of recent hemorrhage were included in the trial of which 129 were peptic ulcers (the rest were mostly erosions or Mallory Weiss tears). Stratification was in 3 groups – spurting arterial hemorrhage, active bleeding (non-spurting) and non-bleeding (red clot or visible vessel). The results (for ulcers only) are shown in Table 5.

Swain (12)

Our trial in London is ongoing, and only preliminary results are available at present. From 259 unselected admissions for upper GI hemorrhage, peptic ulcers were seen in 112. All 55 with SRH accessible to laser therapy were included in the trial (20 were inaccessible, 37 had no SRH). Stratification was in 3 groups – spurting arterial hemorrhage, visible vessel not bleeding and other SRH (bleeding or not bleeding). The results are shown in Table 6.

MacLeod (13)

This trial from Glasgow was limited to patients with major blood loss from peptic ulcers (shock or Hb less than 10 g/dl) and identifiable visible vessels or red or black spots in the ulcer crater at endoscopy (bleeding or not bleeding). From 657 unselected patients, 184 had peptic ulcers. Fourty one fulfilled all the criteria for inclusion and had lesions accessible to laser therapy. None of the 25 with red or black spots rebled (treated or untreated). The results for those with visivle vessels are shown in Table 7.

The first two of these trials (9, 10) were carried out on protocols similar to that drawn up by the American Society of Gastrointestinal Endoscopy (ASGE). The main criteria for entry were a large initial bleed and active bleeding seen at endoscopy without any specific comments on the precise nature of the bleeding point within the ulcer crater nor on how often the ulcer crater could be fully visualised. Both these trials produced negative results.

In the nest trial (11), the nature of the bleeding point was somewhat better defined although all actively bleeding ulcers other

than those with obvious spurting arterial hemorrhage were grouped together. Also, non-bleeding visible vessels were grouped with other ulcers with overlying clot in which the crater was not full visualised, making it difficult to assess the true effect of trea ing vessels not bleeding at the time of endoscopy. Nevertheless, benefit was shown in those with non-spurting bleeding.

The two most recent trials (12, 13) defined the bleeding point precisely in all cases. Both are ongoing, but the preliminary results suggest strongly that when a high risk group of ulcers is clearly defined and endoscopic laser therapy can be directed at t exact source of hemorrhage there is a definite benefit. The resul from all the Nd YAG trials are summarised in Table 8. To date, th number of patients included with precisely defined lesions is toc small to comment on the mortality.

These trials have shown a benifit for both Argon and Nd YAG lasers particularly in selected high risk cases. The way in which each trial was carried out makes an exact comparison between the lasers difficult, but Table 9 shows the results for all ulcers wi accessible visible vessels which were randomized in all the trial

The control groups are very similar, but laser treatment was successful in 84% with the Nd YAG and only 66% with the Argon. Having carried out trials with both lasers personally, it is my impression that hemostasis is more effective with the Nd YAG and these results support that conclusion.

With the ready availability of various forms of endoscopic dia thermy, it is surprising that no controlled trials comparable to the laser ones have been carried out. The only controlled study reported to date with diathermy is that of Papp et al. (14). Four patients with visible vessels treated with monopolar electrocoagu lation did not rebleed whereas 4 comparable controls all rebled. Larger studies are needed.

Despite several encouraging anecdotal reports on the use of lasers to treat variceal hemorrhage, the only 2 controlled studie have given negative results. Ihre et al. (9) included varices in their laser trial and the results are shown in Table 10.

Table 8. Combined trial result for Nd YAG laser (peptic ulcers only).

	Ihre	Escourrou	Rutgeerts	Swain	MacLeod
No of patients randomized	25	75	106	61	29
Major bleed only	-	-	-	-	-
Active bleeding only	-	-	-	-	-
Active bleeding + other SRH	-	-	-	-	-
Focus on nature of bleeding point	-	-	-	-	-
Benefit from laser	No	No	Yes	Yes	Yes

Table 9. Combined results for ulcers with accessible visible vessels.

	LASER		CONTROL	
	Total	Rebleed	Total	Rebleed
Argon	62	21(34%)	63	40(63%)
Nd YAG	25	4(16%)	28	20(71%)

Table 10. Trial results for varices — Ihre et al.

	Total	Rebleed	Died
Laser	3	2	2
Control	5	3	3

Table 11. Trial results for varices — Fleischer.

	Total	Endoscopic hemostasis	Rebled or ongoing bleed	Died
Laser	10	7	7	4
Control	10	0 (4 stopped with pitressin)	7	7

Fleischer (15)

Fleischer et al. carried out a controlled trial of the treatment of actively bleeding varices with the Nd YAG laser and the results are shown in Table 11.

Thus, although the laser was better in achieving immediate hemostasis, there was no significant difference in the final outcome.

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8a. TREATMENT TECHNIQUES FOR MASSIVE UPPER GASTROINTESTINAL BLEEDING. GENERAL CONSIDERATIONS

R. Dwyer

It's an honor to take this opportunity to share with you things that I have been working with for nine years. Lasers will have a bigger impact than X-rays by 10 or 15 times in the practice of medicine. X-rays cut across all specialities and all fields. It's used, however, by one small group of people. Lasers cut across all fields and will be used by all fields.

In therapeutic endoscopy, you have to develop a surgical approach. You have to become familiar with new types of equipment. In essence, lasers are light hemostats. We have a hemostat that delivers its coagulation potential through a fiberoptic instrument. Physical room changes must be tailored for a suite. We can no longer do procedures in the single-bed patient room, squeeze in along the wall and slip your scope in. That's inadequate. We need the same things that standard operating rooms would have for critically ill patients. Techniques of use are, of course, tricks of the trade and everybody has to be taught how to use the equipment and treat the patient with this equipment.

The surgical approach means that you've got to be available. If somebody actively bleeds for a half an hour to an hour, you ought to go in, endoscope the patient, make the diagnosis and perform the treatment. Compare bleeding internal and external lesions. The difference between a scalp laceration and a bleeding internal lesion is accessibility. We wouldn't treat a scalp laceration by watching it hemorrhage, so why treat internal bleeding differently? The ability to do emergency endoscopy is 90% of the procedure, that is being able to isolate the source and then shoot it. Aggressive treatment for bleeding and shock with a team approach is important.

New equipment, special lavage techniques and atmospheric vacuum suction in the room is important. Isolation of the bleeding point

with either a gas jet or a water jet can be done with special scopes and equipment as Dr. Johnston described.

Adequate room area is 250-350 square feet. Anesthesia capabilit must be present. You have to be able to intubate and have the anesthesiologist help manage people that are having active bleedir This involves monitors, defibrillators, crash carts – exactly like the Operating Room. A Xenon light source is helpful for good visualization. Stabilize the patient's blood pressure if reasonable, however, occasionally we must proceed with endoscopy without any anesthesia. Lavage by saline by either gravity or suction helps tc evacuate the stomach and isolate the bleeding sooner.

Therapeutic endoscopy can involve multiple passages of the scop as much as six times during a single procedure and then a lavage tube to follow each time. You have to be able to evaluate the powe of your laser while shooting at the tissue. If you don't see the effect expected for the power setting that you have, you should check your system for problems. You could have a broken fiber upstream or improper setting of the laser controls.

Multiple treatments sites are usually required to control upper gastrointestinal hemorrhage; rarely will there be an isolated single bleeding source. There is frequently one major and several minor oozing areas to be treated. Treatment site technique involv shooting around the lesion and below the lesion in actively bleeding esophageal varices. Lesion cooling is done afterwards by irrigating with saline or water.

In early experiments, we dissected the groins of dogs, isolate arteries and measured the external diameter of the artery. Then, used an iris scissors to cut a side hole to create bleeding. An Argon laser can routinely coagulate a 1.5 mm artery and a Nd:YAG laser can coagulate a 4 mm artery. Therefore, YAG can coagulate bigger bleeders than Argon.

There are three basic medical lasers – Co_2, Argon and Nd:YAG. The YAG laser can be used in urology, pulmonary and gastroenterology for ablation of tumor and gastrointestinal bleeding. Argon lasers are used in dermatology, ophthalmology and gastroenterolog CO_2 lasers are used in multiple specialities – neurosurgery, plastic surgery, otolaryngology and many more.

Light penetrates tissue to different depths independent of power. That means that if you have one wavelength, you may only penetrate superficially while another penetrates very deeply. The tissue effects are totally different. The only way you can effectively perform coagulation is by deep laser penetration. The Argon burn pattern is basically cylindrical and does not extend much beyond where the burn is. The burn of a YAG laser shows deep coagulation necrosis with full coagulation of deep-seated blood vessels without much vaporization. The burn pattern is different than the Argon and looks like a piece of pie. That's because the YAG laser has a unique property called "scatter". Once the laser light of YAG enters the tissue, it then scatters sideways in addition to penetrating straight down. We use the YAG scatter to coagulate the bleeding blood vessels by actually not shooting them directly, but by shooting next to them. The flow of blood acts as a heat sink to burn in the tissue because there's too much blood flowing. All you're doing is making clots. In this situation we shoot away from the flowing blood and into nearby tissue, hoping to scatter and coagulate feeding vessels.

Special scopes with large suction channels or with multiple small channels are useful in therapeutic endoscopy. Large bore lavage tubes are useful to irrigate large volumes of fluids and evacuate large quantities of blood and clots. Intravenous vasopressin by bolus of 10-20 units during massive bleeding episodes from ulcers or varices will assist in coagulation by reducing the volume of blood hemorrhaging and clear the treatment site temporarily.

Post laser treatment, the patient should be NPO. A clear liquid diet can with antacids be given in a day or two. I don't monitor the GI bleeding by nasogastric tubes. They tend to knock off the clot, cause erosions and increase rebleeding. Of course, cimetidine is given during hospitalization and if there is a gastric or duodenal ulcer, I like to keep them on cimetidine until it's healed totally. Nd:YAG laser endoscopy can be used to effectively control 90% of unselected bleeding patients, combining a diagnostic with a therapeutic procedure which I think reduces the number of blood transfusions, morbidity and mortality.

8b. SPECIFIC TREATMENT TECHNIQUES FOR MASSIVE UPPER GASTROINTESTINAL BLEEDING

J. Johnston

The management and endoscopic treatment of patients with massive upper gastrointestinal bleeding is difficult and complex. Before any form of invasive therapy can be safely considered, the patient must be resuscitated and stablized. Two or more large bore intravenous catheters may be required for replacement of fluid, colloid and blood. Central venous pressure or Swan Ganz catheter placement may be needed to monitor blood volume. Coagulopathy should be corrected when possible. Safe transport to the laser unit may present special problems, especially when long distances are involved. At times, patients are bleeding too rapidly to be considered for transfer between hospitals, and immediate surgery may be the best option. Several hours may be required to prepare for and perform endoscopic therapy. Such delays may be excessive for massively bleeding patients who are candidates for emergency surgery.

Whereas elective laser therapy of angiomata or tumors can be safely performed in a gastrointestinal endoscopic unit designed for diagnostic procedures, a special environment is needed to handle a massively bleeding patient. One should realize that even though bleeding has stopped temporarily, endoscopic treatment of a non-bleeding visible vessel may instantaneously induce massive hemorrhage. The special treatment facility may be a modified endoscopic unit, an intensive care unit area, or an operating room, depending upon the local hospital situation. In my community hospital, each of these 3 areas has electrical and plumbing connections for a movable Neodymium-Yttrium Aluminum Garnet (YAG) laser. Each area has adequate space (at least 150 square feet) and lighting, a tilting endoscopic table or stretcher, connection for an anesthesia machine, EKG and blood pressure monitor and display, and crash cart.

In addition to a fully equipped endoscopic cart, another cart carries special laser items such as refrigerated water, large lavage tube and funnel, water pik irrigation device, spare laser fibers with repair kit, and tackle box which includes protective laser eyepiece and goggles, endoscopic connectors, medication (glucagon, vasopressin, norepinephrine) and other accessory items.

During therapeutic endoscopy, at least one qualified assistant must care for the patient, including monitoring blood pressure, pulse, cardiac rhythm, respiratory status, central venous pressure and urine output, as well as administering necessary medication and blood products. This assistant may be a registered nurse or housestaff physician, but in my community hospital, this role is best filled by a nurse anesthetist, supervised by an anesthesiologist. The capability for rapid endotrachael intubation will be needed if aspiration threatens, such as during copious large tube gastric lavage. Overall, 18% of my patients with massive hemorrhage required intubation, and half of those intubated were given a light general anesthetic. A surgeon should be on standby in case urgent laparotomy is needed for uncontrolled hemorrhage.

Before applying any endoscopic hemostatic therapy (laser, electrocautery, heater probe, etc.), the exact point source of bleeding must first be localized and prepared for treatment. This often requires more time and effort than the actual treatment itself. There are differences of opinion regarding the usefulness of routine gastric lavage prior to endoscopic therapy. If gastric clots are excessive, a large bore (e.g. 56 French) tube may be passed for lavage with 500 to 1000 cc aliquots of cold water through a funnel, followed by gravity drainage. Lavage with 10 or more liters of fluid can be performed in a short period in this manner. However, the definite risks include pulmonary aspiration and induction of mucosal suction lesions which can bleed or be confused as the bleeding site. Therefore, I prefer to initially endoscope the patient with a therapeutic endoscope that either has two suction channels (2.8 mm) or one large channel (3.5 to 5.0 mm). The latter is particular useful for removing large blood clots and often fresh bleeding can be localized to one area of the upper gastro-

intestinal tract without any lavage. Changing the patient's position may be very helpful, as reported by Gaisford (1). In the left lateral decubitus position for routine endoscopy, the fundus and greater curvature of the upper stomach are dependent and may be obscured by clots or blood, but the esophagus, gastric lesser curvature, antrum and much of the duodenum can be examined. By rolling the patient to the right lateral decubitus position, blood clots shift dependently and inspection of the upper stomach and fundus is possible (see Figure 1). By rolling the patient to the supine and prone positions, inspection of the anterior and posterior walls respectively is possible. Since the danger of aspiration is significantly increased with these position changes, endotrachael intubation for protection of the airway should be considered. Elevation of the head by reverse Trendelenberg is especially useful with massive esophageal bleeding, if systemic blood pressure can be maintained in this position.

Endoscopic washing is greatly facilitated by a water pik device. This can be directed through a separate forward directed irrigation channel of several new therapeutic endoscopes or through an irrigation catheter. Just prior to endoscopic treatment, small adherent clots resistant to washing may be removed by suction, polypectomy snare or tripod grasper. However arterial spurting may result from clot removal, and the endoscopist must be prepared for immediate treatment.

Coaxial CO_2 or air gas jet is useful to blow away overlying unclotted blood from the target site. An effective coaxial gas or water jet is essential for effective treatment of actively bleeding lesions with argon laser, because of its selective absorption by red pigment such as blood (2). In contrast, the YAG laser wavelength allows penetration through some overlying blood or small clots, and coaxial gas or water is not required for its effectiveness (3). For treatment of actively bleeding lesions with either argon or YAG laser, coaxial gas facilitates aiming and keeps the catheter clear of debris or blood.

Improved endoscopic methods for removing large gastric blood clots are needed. Perhaps agents to selectively dissolve blood clots could be used, although exacerbation of bleeding from

a partially clotted vessel might be expected. Some other mechanical or ultrasonic device might be developed to breakup large resistant clots. Alternatively, a large overtube might be useful for repeated passage of the therapeutic endoscope or lavage tube.

Laser energy is best applied to a target lesion en face. With angulated orientation such as in the esophagus, gastric lesser curvature, or postbulbar duodenum, a sideviewing therapeutic duodenoscope can be effectively employed. Some newer bipolar electrocautery or heater probes are designed to coagulate with the tip en face, as well as with the side tangentially.

Certain ancillary measures may be useful during endoscopic therapy. Intravenous glucagon reduces excessive gastrointestinal motility. Local submucosal injections of norepinephrine or vasopressin may temporarily reduce rapid bleeding. Brunetaud has also used irrigation with very cold water to slow the bleeding rate (4).

There are some differences of opinion about the best technique for treatment of actively bleeding lesions with lasers and other thermal devices. Techniques are not standardized. I prefer to initially apply YAG laser pulses circumferentially 2 to 3 millimeters around the target vessel. This creates an edema cuff within one or two minutes which serves to increase gastric wall thickness and may slow the bleeding rate by extrinsic vessel compression. At times, rimming the bleeding point will coagulate the bleeding vessel at a peripheral point. However, if bleeding continues despite circumferential application, treatment may have to be directed closer to the bleeding vessel. Power density should be adjusted to avoid vaporization or destruction of the vessel wall which will increase the rate of bleeding. Rutgeerts prefers to start with direct YAG treatment at the bleeding vessel (personal communication). In contrast, Papp (5), using monopolar electrocoagulation, and Klass (personal communication), with lasers or monopolar electrocoagulation, feel that thermal energy should never be applied directly to the precise bleeding point. If technically possible, coagulation of the bleeding vessel at sites proximal and distal to the bleeding point is clearly preferred. Ideally, an endoscopic device will be developed to detect the precise location of

the underlying vessel, allowing more efficient treatment efforts.

With the YAG laser, most investigators employ high power (60 to 90 watts), short (0.5-1.0 second) pulses. Treatment distance varies according to the endoscopic situation and laser beam divergence, but 1 to 3 cm is a comfortable endoscopic treatment distance. Coaxial CO_2 gas jet may make the treatment easier, but is not essential for use with the YAG laser. Excess gas introduces the potential hazards related to gas insufflation (see Chapter 14).

Laser light is absorbed by tissue and heat results which produces tissue coagulation or vaporization, depending upon the temperature attained (see Chapter 4). Laser wavelength determines the depth of tissue penetration. Because there is no accurate endoscopic thermometer to monitor tissue heating, therapy is therefore empirical. The energy deposited in a given volume of tissue over time is a major determinant of heat produced. Most tissue factors such as blood flow, tissue thickness and heat conduction cannot be controlled but influence results. For example, if the desired coagulative effect is not attained, there may be a large underlying vessel acting as a heat sink. Of the controllable laser variables (Table 1), power, time and total energy can be precisely controlled, and are displayed on the laser console. For hemostasis with YAG laser, power is commonly varied over a twofold range (50 to 100 watts).

The more important determinants of tissue heating, however, are power density and energy density, which are the amount of power or energy applied to a given target surface area. For example, a 50 joule pulse of YAG laser energy applied to a large area may barely warm the surface, whereas the same pulse applied to a tiny area will vaporize the tissue. The light beam exits the quartz lightguide (0.6 mm diameter) in a conical fashion with a certain divergence (e.g. 10°). The laser light produces a spot on the target surface and the size of the spot depends upon the treatment distance (Figure 1). The power and energy applied to the spot area defines the power density and energy density respectively. Unfortunately, there is no good endoscopic "ruler", and it is very difficult to endoscopically assess spot size or treatment distance. Power

Figure 1. Diagram of the upper gastrointestinal tract, noting effect of position upon dependent pooling of blood and clots.

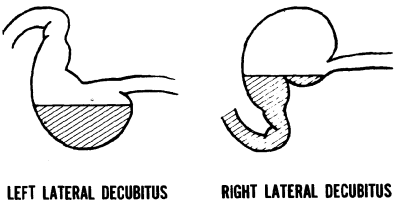


Figure 2. Diagram of a divergent laser light beam, creating laser spots of increasing size with greater distance of the lightguide from the target.

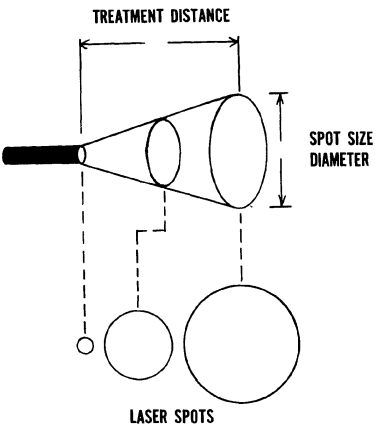
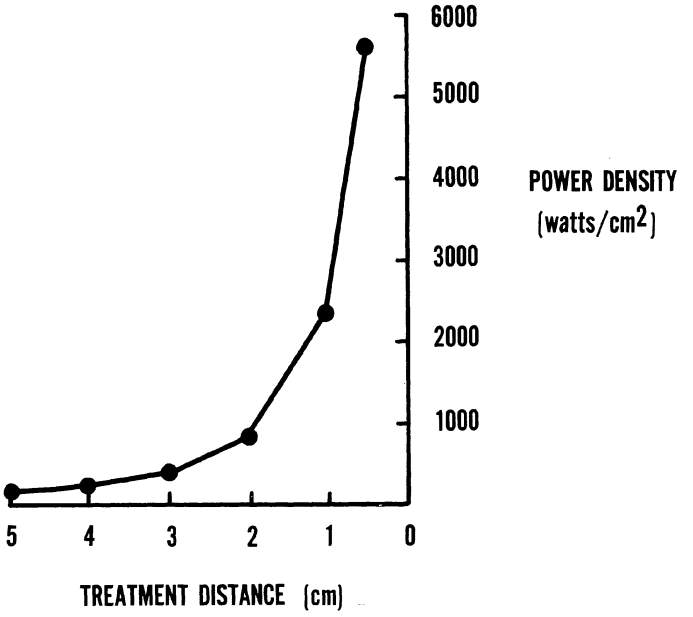


Table 1. Important laser variables

Power (watts) x Time (sec) = Energy (joules)
Spot Size $\propto$ Treatment Distance, Divergence Angle
Power Density $\propto$ Power/(Spot Size Radius)^2
Energy Density = Power Density x Time

Figure 3. Relationship between laser power density and treatment distance, assuming constant power setting of 75 watts.



density (see Table 1 and Figure 2) may vary tremendously over the treatment range: next to the mucosa, spot size diameter is 0.6 mm; at a distance of 5 cm, spot size is 9.4 mm (15 fold range). However, power density is inversely related to the square of the spot radius. As spot size diameter varies 15 fold, the power density actually varies 225 fold (see Figure 2).

Figure 3 depicts this relationship between power density and treatment distance. For effective coagulation with the YAG laser, the operator should stay in the 500 to 1000 watt/cm^2 power density range, occasionally up to 2000. Above that range, tissue vaporization occurs. As depicted in Figure 3, changes in treatment distance between 2 and 5 cm produce relatively small changes in power density. In contrast, for treatment distance less than 1 cm, truly dramatic rises in power density occur with small changes in treatment distance. At a treatment distance of 0.5 cm, power would have to be reduced to 12 watts to maintain a power density of 1000 watts/cm^2. If the laser fiber tip inadvertently touched the mucosa while firing with 75 watts, the resultant power density would be in excess of 25,000 watts/cm^2! Avoidance of excessive power density is critical. For example, if treatment in the duodenum demands a short treatment distance of one centimeter or less, then the power output should be reduced accordingly. The currently available YAG laser lightguide has no safeguard to prevent accidental contact with the mucosa while firing the laser. We have suggested that a 6 mm catheter hood be used to prevent excessively close tretment distance (2). One could also develop a larger (e.g. 2 mm) quartz lightguide that would assure a safer minimum spot size. At present, the operator should pay close attention to endoscopic spot size and treatment distance. When one is uncertain about treatment distance, it can be gauged by lightly touching the adjacent mucosa and then withdrawing the catheter 2 cm before firing.

Regarding YAG laser treatment technique, laser pulses are applied near or at the bleeding site to produce a visible coagulative effect. In animal work, the operator should learn to recognize and avoid visible erosive or ablative effects. Ideally, laser pulses are applied until the bleeding stops. Whereas low pressure capillary and venous bleeding can often be stopped

quickly, high pressure arterial and venous (e.g. portal hypertension) bleeding may be difficult or at times impossible to control with the laser.

What options are available to the operator when YAG laser treatment does not produce hemostasis? Higher power (90 to 100 watts), longer pulses (1 to 2 seconds) and shorter cooling time can be used to further increase tissue temperature, especially when one suspects a large vessel acting as a heat sink. The treatment field can be enlarged in an effort to coagulate the feeding vessel at the periphery. Waiting periods during treatment are most important. Arterial bleeding is often intermittent in nature, hence one may see spontaneous temporary reduction in bleeding rate. Additionally, an adequate waiting period allows maximal time for tissue swelling and edema which may reduce vessel bleeding by a tourniquet effect. Ancillary measures such as local submucosal injection of norepinephrine, vasopressin or perhaps a sclerosing agent might be considered.

Ultimately, treatment decisions for the patient depend upon the risk to benefit ratio. The risk of treatment increases in proportion to the energy, power density, and temperature produced. Investigators have not suggested an absolute upper safety limit on the energy applied during a given treatment. Cases must be individualized. For example, a young healthy person bleeding from a peptic ulcer should not be subjected to excessive laser-related risk when surgery can be performed with a low risk. In contrast, a prolonged laser treatment may be appropriate when treating an unacceptably high risk patient with potentially reversible medical problems and exsanguination from a fundic stress ulcer.

Of my first 108 YAG laser treatments of gastrointestinal bleeding (6), 38 were for massive active bleeding of "surgical" magnitude, 10 were for active bleeding of lesser rate in very high risk patients, 3 were repeat treatments for rebleeding, and 57 treatments were applied to lesions which had stopped bleeding but were likely to rebleed (angiodysplasia - 47, ulcers with a visible vessel - 9, sessile colon polyp - 1). Of the 108 laser treatments, 89 were done in the UGI tract, 17 in the colon, and 2 in the mid small bowel via endoscopy at laparotomy. Patients treated for active bleeding at endoscopy

Table 2. Results of YAG laser therapy for gastrointestinal bleeding.

	Successful Hemostatic Outcome[1]		
Diagnosis	Active Bleeding[2]	Visible Vessel[3]	Total
Solitary GU[4]	13/14	2/3	15/17 (88%)
Multiple GU's, erosions	6/10	1/1	7/11 (64%)
Duodenal ulcer	4/6	1/3	5/9 (56%)
Angiodysplasia	9/9	-	9/9 (100%)
Miscellaneous	7/9	1/2	8/11 (73%)
Totals	39/48 (81%)	5/9 (56%)	44/57 (77%)

Footnotes:

1. The overall hemostatic outcome includes the immediate results of laser therapy, as well as any rebleeding or repeat laser treatment.
2. Patients with active bleeding at endoscopy, treated with laser.
3. Patients with peptic ulcers and visible vessels not actively bleeding at the time of laser therapy.
4. Gastric ulcer (GU).

Table 3. Determinants of treatment difficulty.

Severe rate of bleeding
Endoscopic
    Blood clearance
    Access
    Orientation
Severe vascular disease
Multiple bleeding points
Gastroduodenal artery,
    pancreatic penetration

had a mean transfusion requirement of 9.9 units (5.1 units per 24 hours), and one-third of these patients had active spurting or pumping at the time of laser therapy. The laser was effective in providing overall hemostasis in 81% of patients with active bleeding (Table 2). Laser therapy was more successful with hemorrhage from a solitary gastric ulcer (88%) or angiodysplasia (100%) than with bleeding from multiple gastric ulcers or erosions (64%). The laser was less effective with duodenal ulcers (56%) and ulcers with non-bleeding visible vessel (56%), especially with duodenal location.

For those patients in whom either laser therapy failed or in whom marked difficulty was encountered, there were several common factors (Table 3). Bleeding rate was more severe in patients with unsuccessful laser therapy (mean 9.3 units per 24 hours) than with successful therapy (4.0 units per 24 hours). In 5 patients with massive gastric bleeding, the bleeding site(s) could not be determined due to inadequate removal of large blood clots by gastric lavage. The transfusion requirement during the preceding twenty-four hours ranged from 7 to 34 units in these patients. Gastric blood clots could always be evacuated when bleeding rate was 6 units or less per 24 hours. Endoscopic access to the bleeding site was not possible in one patient due to pyloric stenosis and in another due to anastomotic narrowing. Additionally one patient had bleeding from a gastric suture line abscess that had eroded into a deep artery which the YAG laser could not penetrate. In approximately 10% of cases, tangential endoscopic orientation was a problem, especially along the high gastric lesser curvature, in the postbulbar duodenum, and with one angioma located behind a colonic fold. As one would anticipate, lesions with multiple bleeding points, such as gastric stress ulceration, gastritis, or esophagitis, had a high incidence of failure due to rebleeding from untreated areas. Of four unsuccessful treatments for bleeding duodenal ulcer, at surgery one involved the gastroduodenal artery and two had deep pancreatic penetration with multiple exposed pancreatic vessels in the ulcer bed. I no longer treat deep posterior or inferior duodenal bulbar ulcers with visible vessels using YAG laser, unless circumstances are unusual.

There were four instances in which endoscopic conditions

were ideal but the YAG laser was poorly effective despite prolonged treatment attempts. The explanation may be that a large vessel acted as a heat sink. However, each of these elderly patients had severe atherosclerotic vascular disease, as evidenced by recent aortoiliac or carotid artery surgery, or ischemic colitis. Although atherosclerosis classically does not involve the gastric and duodenal arteries, it may have contributed to the failures in these cases. I wonder if primary vascular factors, with inability of the hardened vessel to shrink and coagulate with heating, may not be more important than is generally recognized.

In conclusion, endoscopic hemostatic therapy is only one part of the total care of a massively bleeding patient, and a coordinated team approach is required. Much time and effort may be required to find the point source of hemorrhage. Suggestions regarding treatment technique have been discussed. Significant experience is mandatory to achieve effective and safe results. At each point during therapy, the risk to benefit ratio must be carefully assessed for the patient being treated.

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9. THERAPY OF UPPER GASTROINTESTINAL BLEEDING: ELECTROCAUTERY VS. ND:YAG LASER – PANEL DISCUSSION.

Moderator: David Fleischer, M.D. Panelmembers: Stephen Bown, M.D., Dean Jensen, M.D., Arthur Klass, M.D., Gustavo Machicado, M.D., Paul Rutgeerts, M.D., Fernando Villa, M.D.

DR. FLEISCHER: Is there a benefit to having all three hemostatic modalities at your fingertips? Would you like to have an electrocautery unit and a YAG laser and an Argon laser?

DR. JOHNSTON: I would like to have all three if money were no object. Lasers are preferable for treating gastrointestinal bleeding. It is a great advantage not to have to touch the lesion that is bleeding. I believe that the YAG laser is more effective for big bleeding lesions. On the other hand I think the Argon is the best treatment method for angiomata. The value of having the electocautery unit is that it is portable and easy to take to the patient's bedside. If I had a bleeding patient in the intensive care unit I would prefer to try using the electrocautery unit there because it is so much more simple to set up. If that did not work I would use a laser.

DR. FLEISCHER: Do the other panel members agree with Dr. Johnston?

DR. JENSEN: I question whether or not the monopolar electrocoagulation is necessary for hemostasis. We have tried the monopolar electrocautery unit very extensively and not found the good result that Dr. Papp and other enthusiasts have found. I think it would be useful to have either a bipolar electrocautery unit or a heater probe in addition to the laser. As Dr. Johnston mentioned it is sometimes very inconvenient to have to move the sick patient down to the laser suite. It would be much easier to take portable devices to the bedside.

DR. BOWN: Instinctively I think that it is likely that an electrocautery unit will be available at a future date that will do a comparable job to the laser. Honestly, however, I do not think it has been found yet. We have done a brief study with the BICAP (multipolar electrocautery unit) and it is quite difficult to use. In our hands it was not nearly as effective as the laser.

DR. FLEISCHER: It is clear that the electrocautery unit has the benefit of being both portable and being less expensive than the laser. Is there anyone who uses both the electrocautery and lasers who thinks the electrocautery unit has technical advantages?

DR. KLASS: We have all three modes in our hospital and there are situations that come up technically, particularly ulcers in the apex of the bulb, where you can't get to endoscope and the fiber to the ulcer. In this situation it has been possible to advance the electrocautery probe out to the ulcer without the endoscope entering the bulb. In this case the electrocautery units is technically more effective than the laser.

DR. FLEISCHER: I would like to establish whether the discussants have a preference between the Argon and the Nd YAG laser.

DR. KLASS: Are you talking only about hemostasis or are you talking about instances other than GI bleeding?

DR. FLEISCHER: Let's limit the discussion to gastrointestinal bleeding. It appears that but two discussants prefer the Nd YAG laser. This seems to reflect the fact that Nd YAG laser has a greater versatility and is a little bit easier to use technically. Dr. Machicad you are one of those who vote in favor of the Argon laser. Could you defend your position?

DR. MACHICADO: In our control studies we were able to obtain 100% hemostasis with the Argon laser and the margin of safety seems saf than that of the YAG. Additonally, for working with angiodysplasia patients the Argon seems more desirable.

DR. FLEISCHER: It should be noted that of the approximately 150 laser unites in the world about 3/4 of those are YAG units. This either reflects physician preference or a greater marketing effort of the YAG manufacturers.

DR. FLEISCHER: After reviewing all the studies about which you reported in Chapter 7, Dr. Bown, how would you characterize the profile of the patients who have benefited maximally from laser therapy?

DR. BOWN: Patients who have either a bleeding peptic ulcer or peptic ulcer with a visible vessel that is accessible to the laser are the ones most likely to benefit. Patients with a visible vessel are high risks for rebleeding (approximately 50%).

DR. FLEISCHER: I emphasize what you pointed out. It should be stated that if you do not see stigmata of recent hemorrhage we do not consider treating a lesion because the incidence of rebleeding is so low. If you saw an ulcer with active bleeding, a visible vessel or a clot you would attempt to treat it.

DR. BOWN: The moral is to wash and wash and wash until you know what is at the base of the ulcer. When we do a laser treatment for an ulcer we pend 3/4 of the time washing. The actual laser treatment time is very small. You have to be persistent and cannot accept the fact that there is an overlying clot blocking the ulcer base. I do not believe that you can do anything useful if you cant't see the exact target site.

DR. JENSEN: I think the visible vessel work is important, but I think there is another dimension. What one would like to know is what is the size of the vessel 1 or 2 cm below the surface. We really don't know very much about what a visible vessel is when we see the small bit of vasculature which pierces the surface. If we knew the size of the feeding vessel we could better estimate the best treatment approach.

DR. FLEISCHER: Dr. Rutgeerts, do you think prostaglandins have an adjunctive role when lasers are used to treat GI bleeding?

DR. RUTGEERTS: I think it is too early to answer the question, but I think prostaglandins might have a role to treat angiodysplasia. Our group has shown that prostaglandins speed the healing of laser induced ulcers. In this regard there may be some benefit to giving prostaglandins before lasers are used to treat angiodysplastic lesions.

DR. FLEISCHER: Assuming that lasers are effective for the treatment of GI bleeding, does a community hospital have enough GI bleeders to justify the cost of the laser.

DR. JOHNSTON: No we don't. I have done hundred treatments in a three year period and that certainly does not cover the cost. Perhaps if you get enough people in other such facilities the lasers it could justify the cost. Our hospital has purchased it as a service item to the community.

DR. FLEISCHER: I suppose, in addition, the hospital has been able to reap some of the benefits from the publicity for your use of the laser.
Dr. Jensen, will you tell us more about your experience with the bipolar units?

DR. JENSEN: The only commercially available unit is made by ACMI and is actually a multipolar probe. It is built on the principal of a bipolar unit, that is the current does not go through the patient but rather from one point in the probe tip to another. I believe the cautery devices are harder to use than either laser and we have had experience with both the YAG and Argon laser. The reason for this is that you have to touch the lesion which is technically a little bit more difficult. Secondly, you have got to get in a little bit better position to coagulate the exact bleeding site. We use the 3 mm BICAP probe in animals and we have been able to stop all bleeding lesions that are accessible to us in the canine model. There are two probe sizes available and I think there is an advantage to the bigger probe, because you can irrigate better, because it is stiffer and because you can tamponade the bleeding lesion with it more easily. Our experience so far has been preliminary, but has been encouraging. Again, to re-emphasize the

principle advantage is that it can be taken to the bedside and it is inexpensive.

DR. FLEISCHER: As of January 1983 the BICAP is available in Europe, but not in the United States on a commercial basis.
Dr. Rutgeerts, have you had experience with the BICAP unti?

DR. RUTGEERTS: have had no personal experience with the BICAP. They are very popular in Europe especially in small town hospitals.

DR. BOWN: We participated in a multicenter clinic trial evaluating the BICAP probe for UGI bleeding. The preliminary results were published as an abstract in Gastrointestinal Endoscopy in May of 1982. Thirty-eight of 44 patients bleeding from a variety of lesions had their bleeding controlled. Eleven patients rebled.

DR. FLEISCHER: Dr. Villa, can you comment on your own experiences with the electrocautery units?

DR. VILLA: We have had reasonably good success with the monapolar unit. A lot has to do with the skill of the individual endoscopist. Recurrence of bleeding has occurred on the average in 45% of the patients.

DR. FLEISCHER: In summary, the following things can be said. To date there is no study that compares endoscopic use of the laser to the electrocautery unit for the treatment of gastrointestinal bleeding. Electrocautery units have the distinct advantage that ≠1 they are affordable and can be take to patient's bedside and ≠2 therefore, less expensive than the laser unit. With regard to the treatment of GI bleeding most of the discussants felt that the laser was easier to use and had certain technical advantages. In rare cases, however, the ability to touch the lesion when it cannot be reached with the endoscope may have some benefit. Not touching the lesion is useful, however, in that after cautery withdrawing the probe may lead to dislodgement of the clot.

There have been no studies comparing Nd:YAG and the Argon laser. For the treatment of angiodysplastic lesions the Argon laser seems more suitable in that the beam is absorbed by the color red, and in addition, the risk for penetration may be less. With regard to

acutely bleeding lesions more physicians prefer the YAG laser to the Argon and this is reflected in the worldwide usage of these t lasers. Stated reasons are ≠1 the ability to treat larger vessels ≠2 the fact that coaxial CO_2 is not mandatory and ≠3 the fact tha treatment distance is not as critical with the YAG as it is with the Argon laser. In the future it is likely that there will be selectable lasers so that the physician can use one wave length c the other in any given point and time.

10. A GENERAL OVERVIEW OF TEATMENT TECHNIQUES – PANEL DISCUSSION

Moderator: Stephen Bown, M.D. Panelmembers: Larimore Cummins, M.D., Richard Dwyer, M.D., Dennis Jensen, M.D., James Johnston, M.D., Gustavo Machicado, M.D., Paul Rutgeerts, M.D., Peter Bright-Asare, M.D.

Although there is a considerable amount of information in the experimental animal literature about the methods for laser photocoagulation of gastrointestinal bleeding, there is some variance among techniques of clinical investigators. Validity of the animal model has been challenged since some of that work was done with hand held lasers rather than with endoscopically delivered laser energy. Additionally, many of the animal bleeding lesions that were produced were made with the standard "ulcer-maker" and this produces a lesion which may be very different than the standard ulcer in humans. Finally, there are no controlled studies showing comparative techniques during treatment of gastrintestinal bleeding in humans. For these reasons it was felt that a roundtable discussion by a group of experienced laser endoscopists might be valuable.

DR. BOWN: I would like to ask the panel to discuss their own parameters for laser treatment. Specifically, what is the appropriate duration, exposure, power and interval between pulses?
Dr. Rutgeerts, you have done a lot of experimental work in animals. Could you tell us how you apply your animal data to humans?

DR. RUTGEERTS: We have studied several power settings and several pulse durations. We conclude that short exposures with high powers cause the most effective hemostasis and the least tissue damage. Using the Nd YAG laser is standard setting for us would be a power of 60 to 70 watts of 0.5 second duration. I believe this is similar to your own experience isn't it, Dr. Bown?

DR. BOWN: We have found the optimum setting to be 70 to 90 watts with a half second exposures.

DR. JENSEN: We are using power settings of 75 to 80 watts with a half second exposure. One of the reasons that we use the half secc exposure is a practical matter. It is hard endoscopically to continue to focus on a lesion for much longer than a half a second without the target moving. Regarding power, we found a variety of settings from the range of 30 to 100 watts had all effectively achieved hemostasis. Another important factor is the time lag between individual pulses. After the laser hits the tissue you wi soon see the development of edema. This increases the wall thickness and lessens the risk of perforation. It sounds like we are a in general agreement for treating ulcers in humans, that is, the range of approximately 75 watts for a half of second or so.

DR. DWYER: I think that if everybody is looking for a magic answer to set your knobs at, you are going to have trouble treating acute gastrointestinal bleeding. All the parameters and numbers that wer mentioned may be meaningless when you are inside a stomach where there is a moving target and the angle of incidents is changing. There is no way of actually measuring what we are depositing in th tissue. What you need to observe is the clinical and endoscopic changes. You need to look for tissue effect. If you are looking to set your knob at a specific setting and then point at the target and step on the foot switch you are going to run into some mistakes. Don't look for specific numbers, but look for results. The endoscopist is the best judge of what happens with all the changes and the angle of incidents, motion and so forth.

DR. BOWN: While we are on the subject of time and duration I think we should focus in on the treatment of the visible artery, either spurting or non-spurting. Again, what are the settings, where do w aim, and what is the mechanism for hemostasis.
Dr. Cummins could you comment on the matter of the treatment of th visible vessel?

DR. CUMMINS: First let me echo Dr. Dwyer's comments about the power and pulse duration. I agree with what Dr. Dwyer has pointed out. As you know my computer model describes specific settings which are very precise. Unfortunately, the laser therapy of gastrointestinal bleeding at this stage of the game is an art and not a science. You must observe the tissue and you may have to increase the power or spot size or duration depending upon the tissue changes. Treatment at this point is truly an art.

With regard to the question of the treatment of a visible vessel inside an ulcer I would do the following: I make a rim around the lesion in an attmept to form an edema cuff. I do it for two reasons. On the one hand I think the edema cuff causes a constrictive effect and tamponades the microvasculature as well as the artery you are aiming at. Additionally, it causes a tissue protective effect by thickening the wall. With the edema you actually dilute the tissue proteins and lipids and this allows the Nd YAG laser to penetrate more deeply interact with the blood vessel and damage the tissue less. After I have rimmed the ulcer I am for the visible vessel itself. I do this as sort of a challenge to see if bleeding will ensue. This may indeed triger bleeding if you vaporize the artery and bleeding may get worse before it gets better. The end point of my therapy is one I can challenge the bleeding site and not cause further hemorrhage.

DR. BOWN: Do you agree with that, Dr. Johnston?

DR. JOHNSTON: That is similar to the method that I use. There is, however, another concept which is at variance to those which some of the other speakers have mentioned. This would involve using a very small low power over a long period of time to get coagulation and shrink the vessel wall. I am not sure why we overlooked this in our original basic work, but we did. If you take a mesenteric vessel in the Lab and turn the power down to about 20 watts, set the tip of the fiber about 2 cm away and apply it for 5 to 10 seconds, the vessel would shrink up and coagulate. I am told that they are using this concept in neurosurgery and there might be some work for us in this area.

DR. BOWN: Do you think that this technique would work with the cas of a vessel inside a chronic ulcer?

DR. JOHNSTON: This is something we ought to look at ourself to see if it works. You could use a large spot size by applying the laser 5 to 6 cm from the ulcer and apply it to the whole general area instead of rimming the ulcer. I don't know if it will work, but tc my knowledge it has not been tried in the past.

DR. RUTGEERTS: When we have a spurting vessel we treat the vessel itself immediately. We treat it until it stops and if it takes 60 pulses and 80 watts then we continue to treat it until the bleedin stops. If there is a non-bleeding visible vessel in an ulcer we first go around the rim of the vessel, but we always complete our therapy by going to the vessel itself. It is my feeling that you should treat the vessel itself and if it starts to bleed it is a sign that your coagulation was not good enough. I think you let th patient go back to his ward if you have not treated the vessel itself you will neeed to have to deal with another recurrent bleedin episode.
I disagree with what Dr. Johnston said about low power and long exposure. I think there is a disadvantage that the build up of temperature in the tissue is much too slow and at the beginning of this treatment you will have a warming up of the tissue causing a vaso dilatation and the bleeding will increase.

DR. BOWN: Would anyone else lik to comment?

DR. DWYER: I think the therapy needs to be structured for the type of lesion in the area where you are treating. The stomach is thick than any of the other gastrointestinal organs and concerns about perforation are less in this area. Therefore, large amounts of energies can be applied with a lot less risk. Regarding the need t individualize each lesion let me use the vascular malformation as an example. I think it makes a difference depending on the size of the vascular malformation and depending upon whether it is flat or raised. If it is raised those are the ones that tend to bleed seve ally and you try not to shoot those directly in the center. First you rim them and them you back up to increase the spot size (which

descreases the energy density) so that in essence you are shooting from a long distance. If we are talking about flat lesions, I usually don't rim the entire lesion.

DR. BOWN: Dr. Machicado, would you like to comment?

DR. MACHICADO: I think I should emphasize that there is not really very good information in the leterature to guide one in this regard. As has been mentioned before you need to individualize and look for tissue effect.
Dr. Johnston will discuss complications of laser endoscopy in another chapter, but I did want to ask the discussants about their own experiences with perforations as a consequence of laser therapy. The quoted figures in the literature are that perforations occur with the frequency of 1 to 2% of patients treated. In my own review of the controlled studies for both Nd YAG and Argon lasers not a single perforation was reported. In my informal conversation with some of the discussants they have mentioned that will fire 50 or 60 pulses at the same spot and in those instances they don't develop perforations. Can someone tell us what the evidence is that we are at risk for perforation? The only person to quote figures about perforation has been Dr. Dwyer. Could you tell us to circumstances underwhich the perforations occurred=

DR. DWYER: I have had two perforations in more than 100 patients treated. One occurred after the first few shots in a severely debilitated woman. I could see the hole almost immediately. The surgeon said that the woman's stomach was like tissue paper in their hands. The second perforation occurred in the stomach of someone I treated very routinely. The perforation occurred two days after the laser treatment. I think it is important to point out that maximal tissue necrosis may not occur for 48 to 96 hours and perforations could occur as delayed events. I don't think that there is really good information to predict what energies will lead to perforations in any individual patient.

DR. JENSEN: I think there is only a very minimal risk of perforation in patients with chronic ulcers because there is always a fibrotic base which gives you a margin of safety. The greatest risk of per-

foration occurs in the colon. This may be particular worse if there is over distention with gas which thins out the colon.

DR. BOWN: Lets turn to another subject. What are the pitfalls for the beginning laser endoscopist? What advice would you give to someone beginning to use the laser?

DR. MACHICADO: I think that the technique requires a fair amount of practice and the person should be a skilled endoscopist to begin with. There is usually some difficulty in estimating distances and it is one of the most important problems a beginner might encounter The other point about techniques is that emergency endoscopy of the acute GI bleeder is very different than a routine diagnostic endoscopy. It is very difficult to isolate the specific bleeding point in some patients and several techniques must be used including large tubes to remove clots, water picks when necessary, moving the patient from his left side to other positions and persistent attempts to find the exact point.

DR. CUMMINS: I would like to make the analogy between beginning laser therapy for acute GI bleeding and beginning sphincterotomies for biliary obstruction. Most of the obstacles that you are going to run into in treating GI bleeding will be basic to the endoscopy of the massively bleeding patient. It is my own feeling that you whould not begin to do sphincterotomies until you have the 15 or 20 minute ERCP technique down cold. If you can't do this you should not try sphincterotomies. I wouldn't advise anyone beginning laser therapy until they are perfectly comfortable with the diagnostic endoscopy of the massive upper GI bleeder.

DR. DWYER: I have a much simplier approach. I give someone a bolt action .22 rifle and tell them to go hunt rabbits. When they come back with 10 rabbits then they are ready to start laser therapy.

DR. BRIGHT-ASARE: Experience in endoscopy is the important factor. Once you are an accomplished endoscopist then you might go to a center and observe experienced laser physicians like Dr. Dwyer, Dr. Fleischer or Dr. Jensen.

DR. RUTGEERTS: Firing the laser is the easier part, preparing the lesion and exposing the bleeding site are far more difficult.

DR. JENSEN: It is important to point out that you need back-up support by trained people if you are going to get a laser. Having a good support team and facility is mandatory. I believe the endoscopic skills that you learn firing the laser in the dog lab are valuable and can be translated to the clinical situation.

DR. BOWN: I would like to add one comment myself. Don't try to do laser endoscopy against the clock. You've got to give yourself time to find the precise target and you musn't fire until you have found it. If you try to do it quickly because you are in a hurry or someone else wants to rush off you'll find out that it will end in a disaster.

DR. DWYER: Therapeutic endoscopy is not like diagnostic endoscopy. When you commit yourself to laser endoscopy you have to make a large investment in terms of time and energy. You have to think like a surgeon. You have to be ready to come in at all hours of the night and you have to be willing to work hard once you get there.

DR. BOWN: In summary the following points can be made. ≠1. Animal work has suggested that laser settings with the Nd YAG laser in the range of 75 to 80 watts for 0.5 seconds and for the Argon laser an 8 to 10 watts for 0.5 seconds seem to best achieve hemostasis with the least amount of tissue injury. However, in humans number guidelines are not nearly as valuable as looking for the tissue effect after the laser has been fired. ≠2. Laser therapy itself is reasonably straight forward. The more difficult aspect of treating the patient with massive acute GI bleeding is clearing the blood from the area so that the exact bleeding site may be seen. ≠3. There is a wide variance among the different discussants as to the exact technique treating specific lesions, for example, an ulcer with a visible vessel. No studies are available to date which are applicable to this question.

11. ENDOSCOPIC LASER THERAPY OF UPPER GASTROINTESTINAL CARCINOMAS

D. Fleischer and S. Bown

BACKGROUND

Esophageal carcinoma is often diagnosed by endoscopy. Of the potentially curative treatments, surgery and radiotherapy are the two most commonly employed. Unfortunately, it is far more common for the treatment of esophageal cancer to be palliative rather than curative.

In a comprehensive review by Earlham and Cunha-Melo[1] which critically evaluated the collective surgical experience for treating esophageal cancer by surgery, it was determined that out of every 100 patients with the disease, 58 will be operative candidates and 42 will not. Of those 58, 39 will have the tumor resected and 19 will be unresectable. Of those 39 that have a resection, 13 will die in the hospital and 26 will leave the hospital. Eighteen of those 26 will live 1 year, 9 will live 2 years, and only 4 will live 5 years (Figure 1). These statistics are compiled from numerous studies that suggest that the 5 year survival for esophageal cancer is approximately 5%. These dismal statistics exist in spite of several decades of curative efforts by surgical resection. Indeed it is commonplace in most institutions that surgery is only considered when the cancer involves the distal one-third of the esophagus. Tumors involving the proximal two-thirds are usually treated by radiation therapy.

In a comprehensive review by Earlham and Cunha-Melo[2] which evaluates the collective radiotherapy results with cancer of the esophagus, they underline the fact that there has been no controlled trial of radiotherapy versus surgery for squamous cell carcinoma of the esophagus. Radiotherapy is

often used for those patients with extensive disease or those who are unfit for surgery. The 1 year survival of 18% is similar to that for surgically treated patients even though this includes many patients rejected for surgery. The 5 year survival is 6%.

Poor survival with both surgery and radiotherapy is the result of both our failure to diagnose these lesions sufficiently early to permit a cure and certain inadequacies of the therapeutic methods available. For this reason, palliative therapy is commonly necessary for esophageal cancers.

Currently existing methods of palliation for esophageal cancer include surgery, radiotherapy, bougiennage, prosthetic stents, and gastrostomy or pharyngostomy. More recently chemotherapy has been used. These are employed to relieve symptoms of dysphagia, odynophagia, chest pain, or bleeding. Each of the palliative modalities may be of benefit in selected cases, but each carries specific limitations. Surgery may not be technically feasible because of the location of the tumor and the condition of the patient. In addition, it has a well-recognized morbidity and mortality. Radiation therapy may take several weeks to provide symptomatic relief and if a recurrence develops after the patient has received a maximal dosage it cannot be re-employed. The attendant side effects of nausea, ill-feeling and potential damage to organs outside the esophagus are still problematic. These latter side effects exist as well with chemotherapy. It is too early to assess the efficacy and safety of chemotherapy because the data is just emerging.[3-7] Bougiennage, with or without the placement of prosthetic stents, has provided symptomatic benefit in certain patients.[8-10] In some patients, the strictured area is too small to allow clinically important dilatation. In others, the tumor distortion makes dilatation difficult or impossible. Complications may accompany this procedure (e.g. perforation, bleeding). Additionally, since tumor is "stretched" rather than destroyed, repeated dilatations are generally necessary. Pharyngostomy or gastrostomy

open an avenue through which nutrition can be poured into the gastrointestinal tract but they deprive the patient of the pleasure of ingesting food and have limited patient appeal. For these reasons, any new form of palliation that may be effective should be studied critically to determine its efficacy and safety.

Endoscopic management of esophageal cancer has several appealing aspects: 1) It averts the need for surgery and general anesthesia with their attendant morbidity; 2) It diminishes considerably the likelihood of systemic side effects; 3) It can be performed under direct vision; 4) Unlike radiotherapy, there is no maximum dose, so that if the tumor recurs in the same area, re-treatment can be performed. It is limited in that it does not affect pathologic tissue outside the gastrointestinal lumen and in that regard it is generally palliative.

As discussed by Cummins (Chapter ?), the physical and histologic effect of the laser tissue interaction is temperature dependent. At temperatures in the range of 60^{o}C, a coagulative effect is achieved. At higher temperatures in the range of 100^{o}C vaporization occurs and there is tissue ablation. Destruction of neoplastic tissue currently involves the use of high temperature attainment, although there is laser effect on cellular components at energies that are not associated with elevated tissue temperatures.

The first animal work using lasers to destroy neoplasms was done in the 1960's[11-23] using a variety of lasers. In 1963 McGuff et al demonstrated that ruby laser could destroy solid hepatic metastatic nodules. He also treated methylcholanthrene induced fibrosarcomas and malignant melanomas in hamsters.[11,12,13] Minton et al described the use of the neodymium laser in 1964 to destroy melanomas, sarcomas and mammary adenocarcinomas in animals.[14,15] McGuff speculates that the laser effect was different from cautery heat in its effect on tumor.[12] The effect was different for different tumors. He felt that the effectiveness was related to wavelength, power density, cumulative energy, pigmentations of

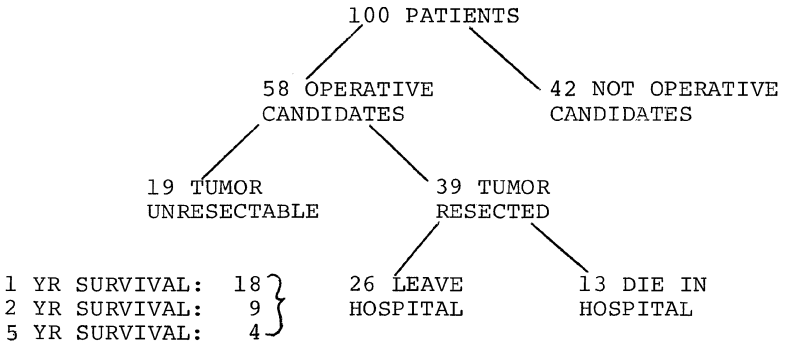
tissue, vascularity of tissue and the ratio of dose and target area to tumor size. Klein et al used a helium-neon and a nitrogen laser to treat melanomas, osteogenic sarcomas, and bladder carcinoma in mice.[16] Minton and Ketcham used a neodymium laser to treat multiple intra-abdominal tumor implants in rabbits[17] and melanomas and sarcomas in mice.[18] Mullins et al destroyed chemically induced primate hepatomas with the neodymium laser.[19] When Ketcham reviewed the role of the laser in cancer he predicted that it would likely become an integral part of many biomedical laboratories[20] because of its ability to destroy selected components of the living cell.[21-23]

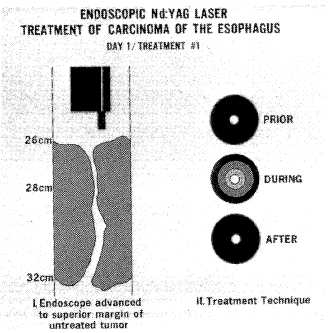
None of these animal studies employed the endoscopic delivery of laser energy to the tumor site. Treatment was delivered to the body externally (skin, breast tumors) or at laporotomy by hand-held fibers or those aimed to a properly positioned organ. Flexible fiberoptic endoscopes routinely allow the physician access to the superior margin of the esophageal tumor or in some cases to more distal areas if the lumen is not dramatically narrowed. Biopsy channels which are present in standard endoscopes provide a conduit through which the quartz fiber carried in a protective teflon coat can be directed at the tumor from the laser photocoagulator. Laser treatment can therefore be carried out under direct vision. Immediate tissue effects can be observed at the time the laser is fired. The technique is described in more detail in a paper by Fleischer.[24] Endoscopic treatment with the laser vaporization and ablation of neoplastic tissue differs from the more commonly employed use of the laser to treat gastrointestinal bleeding endoscopically in that higher power settings for greater durations of time are used. These factors in association with a shorter treatment distance produce a higher energy density and a higher tissue temperature which leads to tissue vaporization.

CLINICAL TRIALS

Each author has used endoscopic laser treatment to obtain palliation in symptomatic patients with esophageal carcinoma.

FIGURE 1 OUTCOME FOR ESOPHAGEAL CARCINOMA





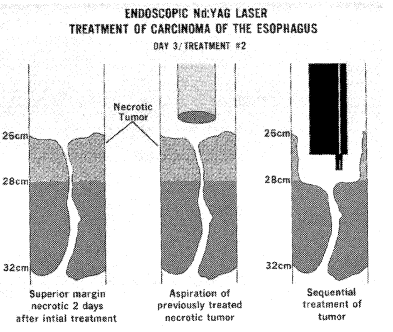


Figure 2. Treatment technique for endoscopic laser therapy of esophageal carcinoma (First treatment)

Figure 3. Treatment technique for endoscopic laser therapy of esophageal carcinoma (Subsequent treatment)

TABLE I QUANTITATIVE GRADING OF SYMPTOMS

Grade	Dysphagia	Odynophagia, Resting Pain
0	None	None
1	Eats solids; food occasionally sticks	Minimal pain; no analgesics
2	Eats only liquids	Moderate pain; occasional analgesics (less than 3 times/day)
3	Cannot eat liquids	Severe pain; constant analgesics required

WASHINGTON VETERANS ADMINISTRATION MEDICAL CENTER TRIAL (FLEISCHER)

Study population

A study was designed at the Washington (D.C.) Veterans Administration Medical Center to treat a selected group of patients with esophageal carcinoma. The following selection criteria were used:

a. Patients with biopsy proven squamous cell carcinoma.
b. In whom it was unanimously agreed upon by the Departments of Surgery, Radiotherapy, Oncology, and Gastroenterology that no curative treatment was was possible.
c. Who were not surgical candidates (i.e. disease in proximal half of esophagus), and
d. Who either developed a recurrence after previous radiotherapy or who were deemed to be better laser candidates than radiotherapy candidates by a joint agreement of both the Radiation Therapy and Gastroenterology Departments on basis of need for rapid relief of obstruction, overall clinical status, ability to undergo a course of radiation, and nutritional status. Therefore it should be understood that in this patient population that no curative treatment existed or that if one did exist it was felt to have specific limitations in the patient under consideration. In this study, esophageal dilatation was employed only as an adjunct after laser therapy.

Baseline information

Before entry into the protocol, the following baseline information was obtained: 1) medical: history, weight, degree of dysphagia, odynophagia and chest pain (Table I); 2) laboratory: complete blood count, multichemical analysis and carcinoembryonic antigen (CEA); and 3) endoscopic: photographs of the lesion, measurement of the tumor and luminal occlusion. These variables were recorded serially.

After each treatment a chest roentgenograph, complete blood count and history were obtained to search for possible complications of the procedure or progression of disease. A barium swallow was obtained before entry into the study and after the completion of laser therapy.

Treatment technique

Endoscopic laser therapy was carried out in a conventional endoscopic suite using an Nd:YAG laser (Molectron) with a power output of 30 to 100 watts. The laser energy was conveyed by way of a quartz waveguide through the biopsy channel of a therapeutic endoscope (Olympus GIF-IT or Olympus GIF-2T). Laser treatment was carried out under direct vision. Patients were prepared with a topical anesthetic and sedated with meperidine and diazepam.

The initial treatment is directed circumferentially around the luminal opening, widening the circle toward the esophageal wall.(Fig.2) The first tissue reaction is a white circular burn where the beam hits the tumor tissue. If the laser beam is continuously focused on the same site, cavitation occurs if the tip of the fiber is close (less than 1 cm to the tissue) and the energy is high (70 to 90 watts). At times bleeding occurs and a black charred appearance develops when the Nd:YAG beam hits the bloody tissue. Treatment continues until the superior margin of the tumor has been treated.(Figure 3) When the treated area is observed 48 hours later, the previously treated area is whitish-yellow, soft and necrotic. The destroyed tumor is evacuated with forceps, polyp grasper or aspiration. Treatment is then begun on the underlying, previously untreated tumor. Laser treatment is continued until the lumen is sufficiently opened to permit passage of the endoscope into the stomach. If necessary, dilatation with mercury dilators is performed.

Patient information

The study population included 13 men and 1 woman. Although carcinoma of the esophagus is more common in males than females, the high percentage of males in this group is

reflective of the general patient population at Veterans Administration hospitals. The age range 49-82 years with a mean of approximately 60 years of age is typical of this disease. As has been underscored before, it was unanimously agreed by the Department of Gastroenterology, Surgery, Radiation Therapy, and Oncology that no curative treatment was available in any of these 14 patients. This was determined by demonstrating disease outside the esophagus or extensive involvement of the esophagus with tumor that correlates with incurable disease. Additionally any patient with distal esophageal carcinoma who could undergo surgery was treated by that method even if the operation was only for palliation. Therefore, the study population selected out a group of patients with esophageal carcinoma who would be less apt to respond well to any palliative method of treatment. Furthermore, 6 of the 14 patients had already undergone radiotherapy so virtually no other treatment was even available save dilatation or gastrostomy and in several of the patients, esophageal dilation had already been attempted and either was unsuccessful or technically not possible. Therefore, it is worth stressing that this group of patients with squamous cell carcinoma is highly selected and the prognosis would be considered dismal by most physicians who are familiar with this condition.

The symptomatic benefit derived by the patients is outlined in Table II. All 14 patients improved with laser therapy. Ten of 14 were asymptomatic after therapy.

The survival in this group of patients was generally 2 to 3 months. Many were still able to eat solid foods until their death. This short survival period should be put into the perspective of this patient population (i.e. several had exhausted all alternative therapies at the time laser treatment was instituted). The emphasis should be placed on quality of life after treatment. Most were able to leave the hospital and most were able to enjoy solid foods. An illustrative case is patient A.D., an 82 year old woman. She was originally thought to have a benign stricture and

TABLE II SYMPTOMS BEFORE AND AFTER LASER THERAPY

PATIENT	AGE	SEX	PREV R-T	DYSPHAGIA		ODYNOPHAGIA		CHEST PAIN	
				PRE	POST	PRE	POST	PRE	POST
WP	60	M	(-)	0	0	0	0	2	0
JK	60	M	(-)	3	1	0	0	0	0
MT	49	M	(-)	2	0	1	0	0	0
LA	64	M	(+)	1	0	1	0	0	0
EZ	59	M	(-)	3	0	0	0	0	0
JH	62	M	(+)	3	0	0	0	2	1
AR	64	M	(-)	0	0	1	0	1	0
CJ	50	M	(+)	1	0	0	0	0	0
MB	65	M	(-)	3	0	1	0	1	0
GL	60	M	(-)	2	0	1	0	0	0
JJ	58	M	(+)	2	0	0	0	3	1
JA	67	M	(+)	2	0	0	0	0	0
AD	82	F	(+)	3	0	1	0	0	0
JM	50	M	(-)	3	1	3	1	3	2

esophageal dilatation eventuated in perforation. After this was treated, she was given a course of radiotherapy but derived little benefit. Attempts at peroral dilatation were unsuccessful. Surgical insertion of an esophageal stent was not possible because of the previous perforation. She was scheduled to have a gastrostomy inserted but was referred for laser therapy instead. She underwent 7 treatments in 18 days with little difficulty. Prior to laser therapy she had complete obstruction and could not tolerate water. After laser treatment, she could eat solid foods. She was able to attend her grandson's wedding. At this writing, 2 months after her last treatment, she is still eating solid foods and has not required further treatment.

The gross and histologic appearances were typical of squamous cell carcinoma of the proximal and mid-esophagus (Table III). The tumors varied in length from 5 to 11 cm. Most caused significant luminal obstruction and typical symptoms.

The mean number of treatments required to obtain relief of obstruction was 5.3. With the exception of patient, J.K., the second patient treated, all patients had 7 or less treatment sessions. The mean time span for relief of less than 2 weeks (11.6 days) compares favorably with radiation therapy. Patients tolerated the treatments well. There was 74 individual treatment sessions in the 14 patients. Preparation was not different from routine upper panendoscopy.

The mean energy delivered per treatment was 4615 w-sec (Table III and Table IV) and the total energy per patient averaged 24, 394 w-sec with a range of 2592 - 70, 217 w-sec. The total energy used correlated with tumor length and degree of luminal obstruction.

Minor complications occurred in a few patients and major complications in 2. Six patients had either lowgrade temperature elevations (<100 degrees F) and/or mild leukocytosis (<12,500/cm^3) after treatments. These are described as complications although it is presumed that these parameters reflect the tissue inflammation and destruction that accompa-

TABLE III DETAILS OF ENDOSCOPIC LASER THERAPY

PATIENT	TUMOR EXTENT (cm)	TUMOR LENGTH (cm)	LUM. OCCLUS. (%)	NO. RXS	TIME SPAN (days)	ENERGY RX. mean (w-sec)	TOTAL ENERGY (w-sec)
WP	25-33	8	60	7	19	3867	27,069
JK	24-31	7	95	13	28	5401	70,217
MT	28-39	11	90	6	13	4769	28,614
LA	25-30	5	95	5	12	4825	24,125
EZ	27-33	6	95	4	8	6214	24,859
JH	28-39	11	25-80	4	7	3383	13,531
AR	29-37	8	20-90	3	5	5541	16,623
CJ	17-25	8	>95	6	14	4419	26,519
MB	20-27	7	20-95	2	3	1296	2,592
GL	19-30	11	90	4	8	6493	25,972
JJ	26-34	8	95	4	7	5145	20,583
JA	30-35	5	85	3	7	4532	13,596
AD	20-29	9	>95	7	18	3627	25,394
JM	27-38	11	90	6	14	5094	30,564

nie the treatment. In no patient was sepsis apparent. Five. patients had pain during 1 or more treatment sessions. This invariably was relieved with increased analgesia. In no patient was hemorrhage a problem.

Major complications occurred in 2 patients. Patient, J.D. developed a tracheo-esophageal fistula 1 week after the last laser treatment. He had a previous course of radiotherapy and some dilatation after his last laser treatment. Dilatation is frequently performed because it can debride tissue made necrotic by laser. Since tracheo-esophageal fistulae may occur in esophageal carcinoma that has not been treated at all and since it can occur as a complication of both radiotherapy or esophageal dilatation, the laser may not have been a factor in this patient. Nonetheless, the fistula developed after laser therapy and it must be considered as a possible contribution factor. The patient's fistula was successfully treated with a perorally placed esophageal prosthesis. Patient, J.M. was being treated by a physician under the supervision of Dr. Fleischer. After the obstructed lumen had been opened by the laser, esophageal dilatation was being performed for purposes of debridement. Immediately after the dilatation the patient developed severe chest pain and a perforation was demonstrated on barium swallow. Surgery was required to drain fluid from the chest. Eventually the patient could swallow without problem. Again this complication occurred in association with the laser therapy, although it was the related procedure, dilatation, which appeared to precipitate the complication.

TABLE IV SUMMARY INFORMATION ESOPHAGEAL CARCINOMA LASER PROTOCOL

	MEAN	RANGE
Age (years)	60.7	49-82
Tumor length (cm)	8.2	5-11
Luminal occlusion (%)	81	20-95
Number treatments	5.3	2-13
Time span (days)	11.6	5-28
Energy/treatment (w-sec)	4615	1296-6493
Total energy (w-sec)	24,394	2592-70, 217

TABLE V

Case	Site	Tumor Length (cm)	Treatment Sessions	Laser Used	Total energy (W-sec)	Recurrence of dysphagia (weeks)	Survival (weeks)
E.P.	Gastric stoma	9	4	Argon	8000	-	14
A.S.	Fundus	8	6	Nd YAG	25000	-	8
A.H.	Mid Oesoph	9	2	Nd YAG	15000	-	5
J.S.	High Oesoph	7	3	Nd YAG	30000	12	16
W.B.	Fundus	13	3	Nd YAG	34000	16	17
J.B.	Gastric stoma	7	3	Nd YAG	26000	-	Well at 13
G.K.	Mid Oesoph	15	5	Nd YAG	Perforation 41000		Well at 8
J.H.	Fundus	4	3	Nd YAG	11000	-	Well at 11
R.S.	Fundus	6	4	Nd YAG	25000	-	Well at 8

LONDON UNIVERSITY COLLEGE TRIAL (BOWN)

As in Washington, patients selected were those considered unsuitable for surgery or radiotherapy. However, the range of tumors was different. This comprised three squamous carcinomas of the upper or middle third of the oesophagus, four adenocarcinomas arising at the gastro-oesophageal junction and two adenocarcinomas obstructing the gastric outflow tract which had recurred after previous resection. Eight were treated with the Nd YAG laser (Fiberlase, Parr & Stroud Ltd) and one with the Argon laser (770 system, Cooper Medical Divices Ltd). Most aspects of therapy were similar to the techniques used in Washington. Treatment was carried out under direct vision using a 400 micron glass fibre passed through the biopsy channel of the endoscope. (Fujinon FG-OPF or UGI-CT) and was directed at nodules of tumour protruding into the lumen at the narrowest point, care being taken to avoid firing at the gut wall to minimise the risk of perforation. To prevent the coaxial carbon dioxide gas used to protect the fibre tip from overdistending the viscus and to allow the smoke produced during therapy to escape, a gas venting channel was provided. This was done either by passing a separate gastric aspiration tube alongside the endoscope when using the FG-OPF or up the single, large (3.7 mm) channel in the UGT-CT. In either case, the venting channel was connected to an underwater drain. A steady flow of bubbles through this provided constant reassurance that the gas escape route was patent.

The patients (all male) ranged in age from 23-88, all

had severe obstructive symptoms at presentation which was relieved by the laser in 8 of the 9. The one patient in whom treatment failed developed two small oesophageal leaks after 5 laser sessions. One of these was in an area inaccessible endoscopically and so there is doubt as to whether the laser caused the leaks, but it was thought wisest not to pursue the treatment. He settled on conservative treatment and later had a successful palliative operation (gastric pull-up procedure). There were no other major complications. All were able to go home after treatment. Figure 5 shows barium studies taken against a 2 cm reference grid before and after therapy in a patient with an adenocarcinoma at the gastro-oesophageal junction. Figure 6 shows barium studies before and after laser therapy in a patient with squamous cell carcinoma of the esophagus. The results are summarised in Table V.

DISCUSSION

In addition to the published data of one of the authors,[26,27] numerous other investigators have begun to treat esophageal carcinoma. Other upper gastrointestinal neoplasms have been treated endoscopically.[27-33] Most of the work was been done with the Nd:YAG laser but some work has been performed with argon laser. Several Japanese investigators have described endoscopic laser therapy with gastric cancers using Nd:YAG lasers. Imaoka et al[27] treated 15 patients with gastric neoplasms. In some patients with early gastric cancers, curative therapy was described. In some patients with stenosing gastric adenocarcinoma treatment was effective in

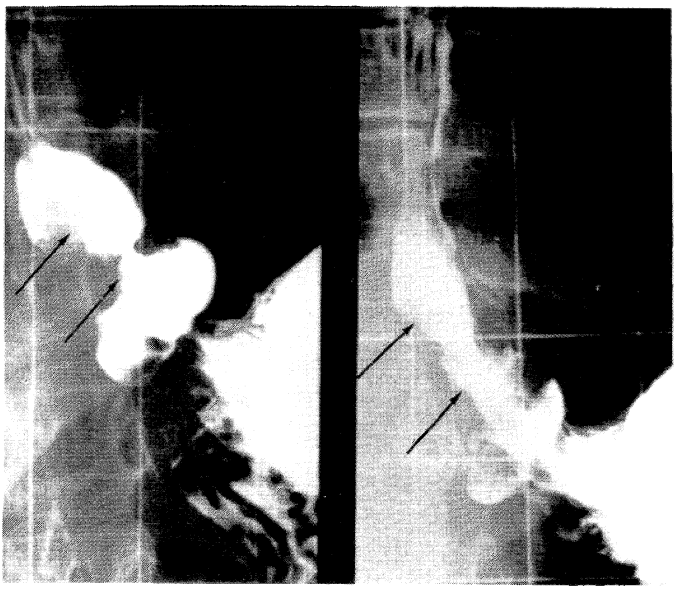


Figure 5. Barium swallow showing adenocarcinoma of gastro-esophageal junction before (left) and after (right) laser therapy. Radiographs are taken against a 2 cm grid to quantitate the size of the lumen

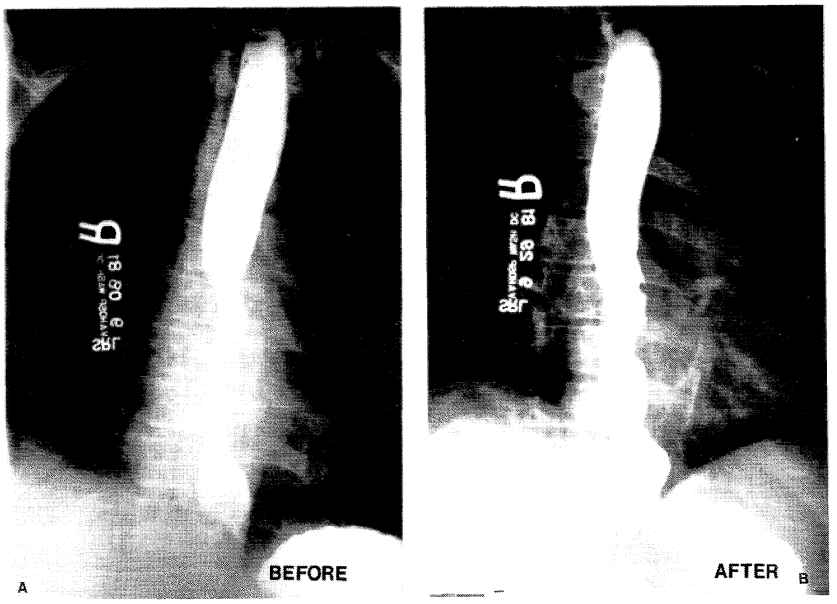


Figure 6A. Obstructing squamous cell carcinoma before (left)

Figure 6B. After (right) laser treatment

about half the patients. In addition to adenocarcinoma they describe effective treatment of gastric adenomas and leiomyomas. Iwasaki et al[29] reported variable effects when gastric cancers were treated by Nd:YAG laser. They suggested that histological tumor type affected the results and that undifferentiated adenocarcinom, responded less well. Mizushima et al[30] reported beneficial effect of Nd:YAG laser therapy for gastric polyps. Ito et al[31] reported on the treatment of 18 "borderline" neoplasms and 16 early gastric cancers concluding that the laser effect may be beneficial. Prunetaud et al[32] in France has used both argon and Nd·YAG laser for palliative treatment of gastric carcinomas. Pichey and Dixon[33] used both argon and Nd·YAG laser treatment to ablate premalignant gastric polyps in one patient. In none of the above studies are complications of laser therapy reported.

The results must be viewed in the light of alternative available treatments. Surgery and radiotherapy can cause severe systemic upset in gravely ill patients and unless they can offer a considerably better long term prognosis to these individuals, endoscopic methods will be superior. The endoscopic technique most widely used at present for the palliation of inoperable malignant dysphagia is dilatation with the insertion of a prosthetic stent. In a recent series of 121 patients deemed unsuitable for surgery, none was rejected as being unfit for palliative intubation, tubes were inserted in 118 and 102 were able to go home. 13 patients died in hospital shortly after the procedure (5 as a result of perforation). Late complications included tube

blockage on 26 complications, 7 cases of tumor growing over the end of the tube and 16 tube displacements.[34] This procedure may require general anesthesia but has the advantage of only requiring one endoscopic session in most cases. Laser treatment with current techniques requires several sessions. No prosthesis is left in situ so there is a possibility that tumor could regrow in the treated area, causing further obstruction, although the necrosis and fibrosis produced by laser therapy makes this much less likely than after simple mechanical dilatation without insertion of a stent. A major advantage of the laser is that it can be used endoscopically in areas such as the gastric outflow tract where prosthesis insertion is impossible without surgery.

Laser treatment for malignant obstruction of the upper gastrointestinal tract is a promising new approach to this difficult clinical problem, but larger studies are needed to assess its merits in relation to the alternative therapeutic modalities available.

TECHNICAL NOTES

The technical methodology is still in its evolution. Endoscopes will need to be modified. A smaller instrument would make treatments technically easier in many strictured areas, especially where the anatomy is distorted. The tips of the endoscopes need to be adapted so they are more resistant to damage from heat and smoke. The laser fibers are also very vulnerable to damage during treatment and various modifications would be valuable. After the tissue is destroyed, the removal is performed by a mechanical technique that can

be modified if the equipment can be developed which would make it easier and more effective. This will need further evaluation.

SUMMARY

Both authors have achieved, symptomatic clinical benefit accompanied by radiographic and endoscopic improvement in all patients described. This suggests that tumor ablation by endoscopic Nd:YAG laser therapy is technically feasible and can be performed with relative safety. The initial clinical results are very encouraging especially when the patient population is considered. In many patients, literally no other method of therapy existed. In several, a dramatic improvement in quality of life was ascertained. Since esophageal carcinoma is a disease with a dismal prognosis for whom palliative therapy is the rule rather than the exception and since all of the existing treatment methods have decided limitations, this method of therapy appears to hold promise. Longer follow-ups will be necessary to determine if these initially encouraging results continue to be demonstrated.

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12. LASER THERAPY OF COLONIC NEOPLASMS

J. Bowers

Laser energy is absorbed by biological tissues and converted to heat, leading to thermal coagulation or vaporization. The depth of tissue injury is predictable and depends mainly on the wavelength of laser light (1,2), as described elsewhere in this monograph. Moreover, it is possible to selectively vaporize or coagulate discrete volumes of abnormal tissue in the gastrointestinal tract while sparing normal surrounding structures. On the other hand, the depth and extent of tissue necrosis after monopolar electrocautery is unpredictable (3), a fact which limits its usefulness in the treatment of neoplasms located within hollow viscera. It is the precise nature of the laser-tissue interaction which suggests its possible application to the local treatment of GI neoplasms.

Experimental studies in our laboratory with Argon laser have demonstrated the feasibility of rapid photocoagulation of large areas of bowel mucosa (Figure 1A). Damage is restricted to the superficial layers, approximately 1 mm deep (Figure 1B), and the integrity of the bowel wall is maintained (1). Argon laser-induced ulcerations heal completely within a few days leaving a normal-appearing mucosal surface (4). Taken together, these observations indicate a potential role for endoscopically delivered laser energy in the management of colonic neoplasms, benign and malignant, in selected patients. Neodymium:YAG(Nd:YAG) laser penetrates more deeply than Argon and frequently causes full thickness injury to normal colon in experimental animals (2,5,6) (Figures 2 A,B). The colonic wall is very thin (1-2 mm) as compared to the stomach or small bowel, because the muscularis

FIGURE 1A. Argon laser photocoagulation, canine stomach, acute. Large mucosal surface area has been easily coagulated.

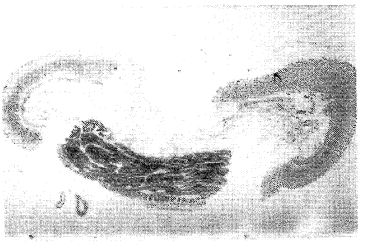

FIGURE 1B. Argon laser ulcer, canine colon, after 4 days. Damage is restricted to the submucosa.

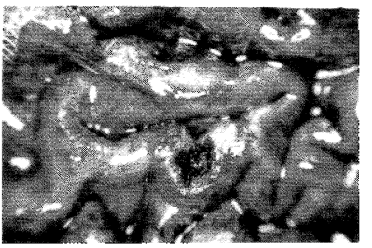

FIGURE 2A. Nd:YAG laser ulcer. canine stomach, acute. Central excavation and carbonization is present.

FIGURE 2B. Nd:YAG laser ulcer, canine colon, after 4 days. Full-thickness thermal injury is apparent.

externa is vestigal in the intraabdominal portion of the colon, being represented by longitudinal bands of muscle known as taenia coli. Moreover, colonic gas distension during endoscopy accentuates this colonic wall thinning. The risk of perforation may be higher with Nd:YAG than with Argon. Notably, colon thickness is likely to be greater in regions of neoplastic involvement, thereby enhancing the safety of Nd:YAG use. The greater penetration of Nd:YAG laser allows for more rapid coagulation of a given volume

of tumor. However, the choice of laser, best methods of treatment and ultimate role of laser therapy in the management of colon neoplasia remain to be determined.

Some benign colonic polyps, because of their size and configuration, do not readily lend themselves to standard endoscopic diathermic removal. Additionally, colon cancers may present with local complications, such as obstruction of bleeding, which require treatment even though the patient may already have disseminated or unresectable disease. Certain individuals with colonic neoplasms, benign or malignant, may refuse surgery or have excessive risk for surgical treatment because of concomitant medical illnesses. Alternative treatment methods are needed for these patients. Accordingly, the results of our preliminary experience in the treatment of colon neoplasia with Argon and Nd:YAG lasers will be presented in this chapter.

I. GARDNER'S SYNDROME

A large kindred affected by Gardner's Syndrome (GS) has been followed at the University of Utah for several years. Nine of these patients agreed to have Argon laser photocoagulation of rectal polyps. Each patient had previously undergone subtotal colectomy with ileorectal anastomosis for treatment of GS. Acute and chronic studies were performed.

A. Methods: Argon laser treatments were delivered via flexible quartz wave guide with low flow, coaxial CO_2 gas or air. The fiber was inserted through a flexible, fiberoptic, therapeutic endoscope which had two channels in order to facilitate gas removal. Treatment distance was 0.5-2.0 cm and power 3-5 watts. Laser energy was applied in a continuous wave mode with pulse durations up to 10 seconds. The equipment used did not permit measurement of total energy delivered; however, a typical 2-4 mm sessile polyp required 5-20 seconds of coagulation. Treatment was considered complete when the entire surface of the polyp had blanched (Figure 3A).

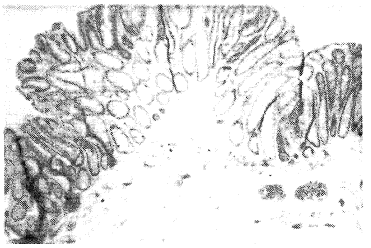

FIGURE 3A. Typical adenomatous polyp from a patient with Gardner's Syndrome.

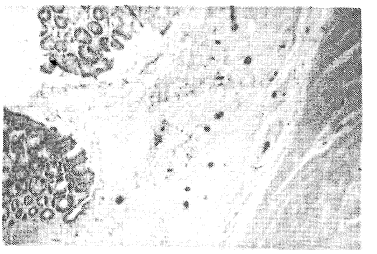

FIGURE 3B. Argon laser ulcer, surgical specimen from patient with Gardner's Syndrome, after 4 days. Damage is limited to the submucosa, and submucosal vessels are thrombosed.

B. Results: One GS patient had been scheduled for surgical removal of her rectum because of inability to control polyp regrowth. Four days prior to surgery 15 rectal polyps were photocoagulated with Argon laser. The surgical specimen was studied histologically and found to show ablation of polyps with thrombosis of submucosal vessels. Tissue injury was limited to the submucosa (Figure 3B).

The remaining 8 patients with GS had 177 polyps photocoagulated with Argon laser as described above. Follow-up endoscopies were performed at 4 and 12 days to assess the tissue effects. At 4 days, the polyps were gone and small superficial ulcerations were present. After 12 days the mucosa had completely healed, and polyps were no longer present. These same 8 patients have continued to return at 4-6 month intervals for coagulation of any new polyps; more than 500 polyps have been removed. Treatments have been well tolerated on an outpatient basis, and no significant complications have occurred.

II. BENIGN COLONIC POLYPS

Twenty-seven benign colorectal polyps have been photocoagulated with Argon laser in 4 patients.

A. Methods: Polyps selected for laser therapy met 3 criteria. They were sessile, more than 5 mm in transverse diameter and not easily removed by standard endoscopic techniques. Argon laser treatments were applied in the same manner as with the Gardner's Syndrome patients. Follow-up endoscopies were scheduled at 4 and 12 months after initial coagulations were completed.

B. Results: Polyps ranged in size from 4-20 mm. All of the treated polyps were absent when repeat endoscopy was performed after four months. One large (20 mm) rectal polyp recurred one year later and was treated with Nd:YAG laser (Figure 4). The remaining 26 polyps have not recurred during observation for up to 14 months.

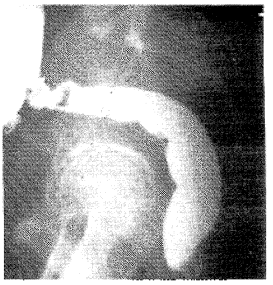

Fig. 4A. Tubular adenoma on anterior wall of rectum in 79 year old man.

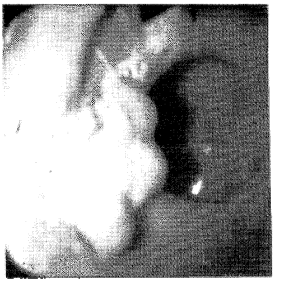

Fig. 4B. Endoscopic appearance of lesion seen in Fig. 4A, pretreatment

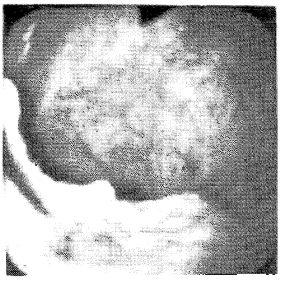

Fig. 4C Endoscopic appearance of lesion seen in Figs. 4A,B, immediately after treatment with Argon laser.

III. COLORECTAL CANCER

Seven biopsy-proven malignant neoplasms of the rectum and sigmoid colon have been treated with Argon and Nd:YAG lasers. Five of these patients had disseminated cancer at the time of laser treatment. The remaining two patients were high risk surgical candidates, and both had refused surgery in any case. The objectives of treatment were three-fold: 1) to reduce tumor size; 2) to relieve or prevent obstruction; and 3) to control hemorrhage.

A. Methods: Argon laser treatments were applied in the same manner as with the Gardner's Syndrome patients. Nd:YAG laser energy was delivered via flexible quartz wave guide with coaxial carbon dioxide gas through flexible, fiberoptic, therapeutic endoscopes at a treatment distance of 0.5-2.0 cm. Power was set at 50-60 watts with the pulse durations up to 2 seconds. Each treatment was considered complete when the entire surface of the neoplasm had been coagulated. Multiple treatment sessions performed at 2-5 day intervals were often necessary in order to achieve the desired initial effect on the tumor mass. The first follow-up endoscopies were performed after one months. Subsequent examinations and treatment sessions were performed at 3-4 month intervals on an outpatient basis.

B. Results: Our initial experience with Argon laser indicated the penetration depth was inadequate to rapidly coagulate large volumes of tumor tissue. Numerous treatment sessions were required, and rapid tumor regrowth was observed. Consequently, the use of Argon laser was abandoned after the first three patients. We now use Nd:YAG laser exclusively in the treatment of cancers. In spite of the theoretical risk of perforation with Nd:YAG laser, no complications have occurred with the use of either laser.

The size of the intralumenal portion of the tumor was reduced in all six patients who were treated for that purpose. None of these patients have developed obstruction or bleeding following laser therapy over the next 1-15 months. No patient has been cured of his or her cancer, but five of the six patients are still alive. One patient died suddenly at home of coronary heart disease.

Two patients treated for incipient obstruction have remained free of symptoms 5 and 15 months after treatment (Figure 5). One patient treated for intractable bleeding remained free of hemorrhage until his death three months later from renal failure due to bilateral ureteral obstruction by tumor. Overall, five of seven patients are alive 1-15 months

(mean 7.6 months) after the initiation of laser treatment. These results are summarized in Table 1.

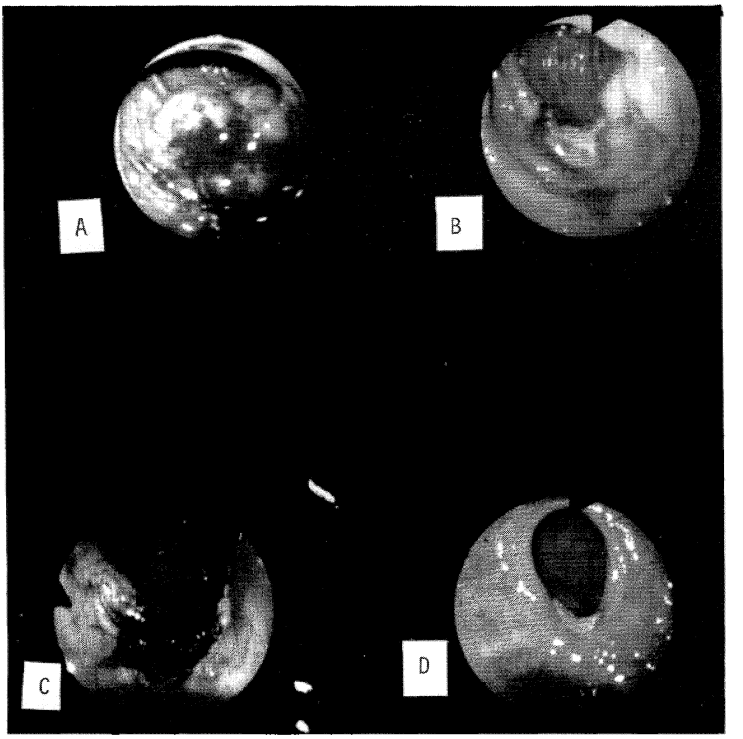

FIGURE 5A. Polypoid adenocarcinoma of rectum in 78 year old man, pretreatment.

FIGURE 5B. Same lesion as in Figure 5A, after partial removal with monopolar electrocautery snare.

FIGURE 5C. Same lesion as in Figures 5A,B, immediately after treatment with Nd:YAG laser.

FIGURE 5D. Same lesion as in Figures 6A,B,C, one month after treatment with Nd:YAG laser.

TABLE 1. Laser photocoagulation for colon cancer.

		indication for Rx			laser Rx's		
location	N	tumor reduction	obstruction	bleeding	Argon	Nd:YAG	Mortality
sigmoid	1	1	1	0	4	2	0
rectum	6	5	1	1	3	14	2
TOTALS	7	6	2	1	7	16	2*

*Causes of death were coronary heart disease and chronic renal failure. The remaining patients are alive 1-15 months (mean 7.6 months) after beginning treatment.

DISCUSSION

The concept of laser coagulation for neoplastic lesions in the colon is attractive, because the extent of tissue injury is more predictable than with electrocautery. The colon, being thin-walled, is subject to perforation if full-thickness thermal injury occurs. Preliminary studies performed in our laboratory demonstrated the safety of Argon laser in normal canine colon. We found that the duration of focal laser irradiation required for perforation was well beyond the pulse durations expected to be required clinically (4). Nd:YAG laser causes much deeper injury to the bowel wall than Argon laser (5) and, the risk of perforation would seem to be much higher. For that reason, we were initially reluctant to use Nd:YAG at all in the colon. However, our experience has shown that Argon laser may not be effective for the treatment of larger deeper lesions, particularly cancers. The use of Nd:YAG speeds treatment and decreases the number of treatment sessions necessary to achieve the initial objectives. We have not had difficulty with perforation when Nd:YAG laser was used on larger, deeper neoplasms. Treatments are begun centrally and care is taken not to irradiate areas of normal appearing colon. Therefore, it appears that the choice of laser depends on the size and configuration of the individual lesion to be treated.

Patients with Gardner's Syndrome and familial polyposis

are highly prone to develop colon cancer at an early age (7). The appearance of cancer is preceded by the presence of numerous adenomas which eventually may become malignant. Total colectomy prior to the development of carcinoma is the most reliable method of preventing death from colon cancer (7). However, some of our patients wanted to retain normal defecatory function and had previously undergone subtotal colectomy with ileoproctostomy. These patients return at frequent intervals to have new polyps removed. In this study, Argon laser was effective and well tolerated when performed at intervals on outpatients with Gardner's Syndrome. However, the long term usefulness of this technique remains to be determined.

Most benign colonic adenomas are easily removed with established endoscopic techniques. Pedunculated polyps can be removed with a monopolar electrocautery snare device (8). Small (less than 5 mm) polyps are easily removed with a "hot biopsy" forceps (9). Larger sessile polyps may be difficult to safely remove because of the risk of perforation, and surgical excision has been the mainstay of treatment for this type of lesion (8). However, some patients may not be good operative candidates because of refusal to have surgery or the presence of severe concomitant medical conditions which pose high operative risk. In this selected patient group laser photocoagulation may prove to be useful. In our study, small, flat lesions were easily treated with Argon laser. Larger polyps may require Nd:YAG, particularly if they recur after initial treatment with Argon laser. The choice of laser depends on the endoscopic surgeon's judgement. In any case, careful long-term follow-up is necessary. Our patients are reexamined at 1,4 and 12 months and yearly thereafter as a general rule. The specific time intervals may be individually adjusted as necessary.

Malignant colonic neoplasms, if small and confined to the mucosa, might be cured with endoscopic laser therapy alone. However, it's not possible to adequately stage colon

cancer by endoscopy alone. The use of laser as the definitive form of treatment must be reserved for those patients who are not surgical candidates. Some patients with inoperable colon cancer may develop local complications such as bleeding or obstruction which have, heretofore, required surgical treatment. Endoscopically-directed laser treatment provides an alternative to surgery for the management of these problems. This may be of particular value because many of these patients have limited life expectancy.

Tumor size is reduced with laser photocoagulation. Moreover, Nd:YAG laser has been effective in the palliation of obstructing esophageal (10,11) and gastric (11) cancers. Our experience in colonic cancer is limited, but it should be possible to prevent circumferential colon cancers from progressing to obstruction by the technique of interval endoscopic laser removal of the intralumenal portion of the tumor. Treatments are easier and better tolerated when performed prior to the development of complete obstruction. Multiple treatment sessions, spaced at 2-5 day intervals are initially necessary. After the initial phase of therapy is completed, interval treatments may be performed at 3-6 month periods. Treatment intervals must be individually adjusted according to the individual rate of tumor growth. Removal of cancerous tissue proceeds more quickly with Nd:YAG laser than with Argon, and we have essentially abandoned the use of Argon in cancer palliation.

Chronic bleeding from friable tumor tissue is occasionally severe enough to require hospitalization and transfusions. Laser energy causes thermal coagulation of small vessels (12) and promotes fibrosis in laser-irradiated tissue (1). Laser photocoagulation has proven useful in the management of bleeding from peptic ulcers (13,14), vascular malformations (15) and a variety of other nonneoplastic lesions in the GI tract. In addition to the single patient described in this report, we have used laser for palliation of chronic bleeding in three patients with gastric, duodenal and biliary adenocarcinomas.

In all three patients clinical bleeding was controlled and the need for transfusions obviated.

Monopolar electrofulguration has been used with considerable success in rectal cancers (16). However, it's use has been restricted to tumors which are below the peritoneal reflection on the posterior wall of the rectum. General anesthesia is required and, as with laser, multiple treatments are necessary. On the other hand, the precise nature of the laser-tissue interaction permits its use in the intraabdominal portion of the colon. Laser treatments may be performed on outpatients with either no anesthesia or simply mild sedation. A note of caution is in order. Even though some patients with early colon cancer may be cured with laser, the use of laser must be regarded as strictly palliative, not curative.

In summary, laser photocoagulation appears potentially useful in the management of selected patients with benign and malignant colonic neoplasms. For the present, it's use in patients with benign colonic polyps should be restricted to those cases where standard endoscopic and surgical techniques cannot be safely applied. In cancers, laser therapy is non-curative but may be helpful in the treatment or prevention of local complications such as obstruction or bleeding.

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13. GASTROINTESTINAL ANGIOMATA: DIAGNOSIS AND TREATMENT WITH LASER THERAPY AND OTHER ENDOSCOPIC MODALITIES

D. Jensen and S. Bown

INTRODUCTION

Acute or chronic gastrointestinal (GI) bleeding and iron deficiency anemia may result from GI angiomata. In this report, specific angiomatouw lesions discussed are Osler-Weber-Rendu (O-W-R) telangiectasia and non O-W-R angiomata including telangiectasia and angiodysplasia. O-W-R syndrome, a disorder of dominant inheritance, was diagnosed in our series (1) when patients had a positive family history; mucous membrane, tongue, and digital telangiectasia; and endoscopically documented GI bleeding from telangiectasia.

Non-O-W-R angiomata were diagnosed when features of O-W-R syndrome were absent but GI angiomata were the source of GI bleeding. The etiology of GI angiomata is unknown but several associated conditions have been recognized. These include valvular heart disease, increased age, collagen-vascular syndromes, renal failure, cirrhosis and previous radiation treatment (1, 2).

Abnormal mocusal and submucosal vessel proliferation characterize O-W-R telangiectasia and other angiomata. The pathophysiology and etiology of these lesions may be related to altered circulatory status as suggested by several factors: 1) the common distribution of GI bleeding angiomata in "watershed areas" of the cecum and posterior gastric corpus; 2) the common association with valvular heart disease; and 3) the improvement or worsening of GI bleeding relative to heart failure (1). In our experience, overt GI bleeding is often associated with increasing size of GI mucosal angiomata; with medication such as anticoagulants, aspirin, non-steroidal anti-inflammatory drugs; and with worsening cardiac dysfunction.

The incidence of O-W-R syndrome in the general population is about 5 in 100,000. In a large series of O-W-R patients, about one-third had severe gastrointestinal bleeding (3). There are no accurat estimates of the prevalence of angiomata (including angiodysplasia) in the general population as a source of significant GI bleeding. Non-bleeding angiodysplasia have been reported to be a common findin in surgically resected cecums and right colons of elderly patients when careful histologic examination and latex injections are performed (4). The prevalence of angiomata and O-W-R telangiectasia as a source for severe UGI bleeding in our series for a large Veterans Administration Hospital and University Hospital is about 5%. For severe lower GI bleeding the prevalence is about 35% for angiomata (5).

Traditional medical management of bleeding GI anigomata includes supportive care, transfusion, correction of coagulation or platelet abnormalities, and treatment of associated conditions such as cardiac dysfunction. Other measures include surgical resection or involved bowel segment, angiographic embolization, and trial of estrogens (3).

METHODS

Diagnosis

Prior to endoscopic treatment of GI angiomata, important diagnostic considerations include their distribution, number, localization as the bleeding lesion, configuration, size, and differential diagnosis.

Distribution. The majority of bleeding angiomata or O-W-R telangiectasia in our patients have been in the cecum, right colon, or posterior aspect of the stomach corpus. Less common areas are the duodenal bulb, post bulbar area, and sigmoid colon. The esophagus and small bowel have been uncommon sources of bleeding.

Number. Often O-W-R telangiectasia and angiodysplasia are multiple. If they are the source of GI bleeding, large circumferential, multiple or contiguous angiomata should be considered for surgical resection. Individual or less extensive angiomata are amenable to endoscopic coagulation.

Localization of bleeding angiomata. The segment of bowel with telangiectasia (O-W-R) syndrome) or individual angiomata causing the GI bleeding should be localized prior to treatment. Emergency endoscopy and/or repeat elective endoscopy after the bleeding stops may be useful for localization of UGI bledding angiomata. Angiomata may be very difficult to distinguish from blood, submucosal lesions or culcers when there is significant, active bleeding. Whether the angiomata are incidental findings or the source of significant bleeding needs to be determined prior to treatment. We do not treat angiomata of the gut unless active bleeding or adherent clots are found endoscopically and no other bleeding lesion is found. For severe lower GI bleeding, emergent colonoscopy after saline or sulfate purge is the best method to localize lesions and identify bleeding sites (6).

Configuration and size often determine the choice of therapy and whether angiography or surgery should be considered. Small (5 mm), flat, discrete angiomata are easier to treat than moderate (5-10 mm) or large (10 mm) sized angiomata. Depressed angiomata may be mistaken for ulcers or erosions particularly if adherent clots are present. Large elevated, or umbilicated angiomata may have extensive submucosal or transmural anastamoses; angiography and surgical consultation should be considered prior to their endoscopic coagulation.

The differential diagnosis of small flat angiomata includes clot or adherent blood, suction artifact, or erosion. Petechiae and submucosal hemorrhages related to thrombocytopenia, sepsis or severe coagulopathy or renal failure can be distinguised by appearance and clinical history. For moderate sized or large angiomata, additional considerations include submucosal vascular tumors, trauma, focal inflammation, ischemia, endometriosis, focal varices or large arteriovenous malformation. Pretreatment barium contrast studies and selective visceral angiography have been useful to exclude non-angiomatous lesions in some patients. Photographs for documentation are also recommended. For non-diagnostic lesions, repeat interval examination and photography are recommended for comparison. Directed biopsy of vascular lesions can be diagnostic because of the resultant increased bleeding and characteristic microscopic appearance (4, 10). I do not recommend this approach for diagnosis of suspected angiomata unless endoscopic treatment can be quickly applied.

Thermal methods for endoscopic treatment

Effective endoscopic thermally active methods for coagulation include monopolar electrocoagulation (MPEC), bipolar electrocoagulation (BPEC), argon laser (ALP), neodymium-yttrium-aluminum-garnet (YAG) laser, and heater probe (7).
The multipolar probe is a type of bipolar electrode. All except the heater probe are commercially available.

There are some unselected, non-randomized reports of GI angiomata and O-W-R telangiectasia treatment with Argon laser (8), YAG laser (9), and MPEC (10). MPEC has been applied via hot biopsy forceps (10), polypectomy snare tips, and monopolar electrodes. We have applied bipolar electrocoagulation and heater probe for angiomata coagulation. All methods coagulate effectively but there are differences in technique of application and depth of coagulation. No long term studies, randomized studies, or controlled studies with any endoscopic thermal method for angiomata treatment have been previously reported. Whether the benefit of endoscopic treatment of the patient with angiomata outweighs the effort, expense, and risk has not been determined or reported previously by any endoscopic method.

Accurate clinical data on perforation rates for different thermal methods during or after angiomata treatment are not available. However, several important lessons have been learned from reported animal studies. Histologic studies in dogs have revealed that the relative depth of penetration and resultant histologic damage for endoscopically treated gastric ulcers in increasing order is Argon laser $\cong$ bipolar electrocoagulation $\cong$ heater probe $<$ YAG laser $<$ MPEC (11). We have gound similar relative damage for treatment of normal mucosa (simulating mucosal lesions such as angiomata) for the canine stomach, duodenum, esophagus, right colon and cecum. The relative thickness of normal canine bowel in decreasing order is: stomach $>$ esophagus $>$ duodenum $>$ right colon $>$ cecum (12, 13). These approximate the normal human bowel relatinships. Age, atrophy, or acute ulceration may decrease wall thickness. Chronic inflammation, tumor or edema may increase bowel wall thickness. Angiomata in patients do not usually increase the bowel wall thickness. Distension of the stomach during endoscopic coagulation (14) and probably distension of any hollow viscus, significantly increases the incidence of

transmural thermal injury. For distensible mucosal lesions such as angiomata, treatment after overdistension should be avoided. The location of angiomata may influence your choice of endoscopic coagulation method. Gastric angiomate are often in the posterior aspect of the stomach. Deep injury from treatment may result in penetration rather than free perforation. Angiomata in the cecum, right colon, or duodenum are often anterior so that transmural injury can cause free perforation.

A careful choice of endoscopic coagulation method and avoidance of distension are recommended. After determination of the limitations and guidelines for effective endoscopic use in canine studies of all available thermal devices (7, 11, 15) we are evaluating Argon laser, bipolar electrocoagulation and heater probe in angiomata patients.

Other measures after endoscopic treatment

Successful treatment of angiodysplasia or telangiectasia depends upon coagulation of the abnormal vessels. Thermal damage results in mucosal and/or deeper damage with erosion and ulcer formation. The more extensive (in surface area and depth) the treatment, the more the tissue damage. Healing and re-epithelialization of the area with mucosa lacking the abnormal vessels is required. Adequate nutrition, oxygenation and supportive medical care are required to aid in healing these induced erosions and ulcers. We often use cimetidine and antacids after UGI angiomata treatment. Routine nasogastric tubes are not used. A program of careful follow-up must be developed for each patient with bleeding GI angiomata. The interval and extent of future endoscopic treatments will depend upon each patient's healing abilities, their rate of growth of new angiomata, and their ability to return for follow-up.

OUR RESULTS

Endoscopic treatment of angiomata in patients with GI bleeding (1)

For treatment of patients with severe GI bleeding from angiomata, we applied endoscopic Argon laser photocoagulation (ALP) using a Cooper Medical 770 unit with 8 to 10 degrees full angle of divergence, 7 to 10 watts, coaxial CO_2, treatment distance of 1 to 3 cm. All

patients with active bleeding or evidence of recent bleeding at endoscopy or colonscopy were enrolled in an elective program of endoscopic treatment and follow-up. Twenty-three patients had 549 lesions of the esophagus, stomach, duodenum, and the colon treated with endoscopic Argon laser. There were two separate patient groups.

Angiodysplasia. Fifteen patients with a mean age of 54 years and with more than 195 units of blood transfused prior to treatment had 154 angiodysplastic lesions treated. Their predisposing medical conditions included valvular heart disease in eight, cirrhosis in three, radiation treatment of a pancreatic malignancy in one and significant renal disease with graft rejection in one. Patient outcome during the follow-up period was compared with the same time period before Argon laser treatment in each patient. During the follow-up period of 12 months (mean), the mean hematocrit rose from 25 to 34 in these patients. The growth of new bleeding lesions varied from three months to 45 months in this patient group. During the follow-up period, there was a reduction in emergency admissions for GI bleeding, total transfusions, and surgery.

Osler-Weber-Rendy syndrome. Eight patients, with a mean age of 63 years and with more than 360 units transfused before treatment had 395 telangiectasias treated with Argon laser photocoagulation. Five had vavlular heart disease. The mean hematocrit in this group rose from 25 to 47 over the follow -up period of 13 months (mean). The growth of new bleeding lesions in this group of patients varied from two to six months. Based on this time interval, a program of elective endoscopy and laser treatment was followed for each patient. During the follow-up period compared with the same interval before Argon laser treatment, there was a reduction in total transfusions, admissions for GI bleeding, and surgery.

There have been no complications of endoscopy or Argon laser photocoagulation in these study patients. Argon laser is safe and effective for the treatment of endoscopically accessible hemangiomata of the GI tract.

Argon laser photocoagulation of bleeding colonic lesions during emergent colonoscopy (5, 6)

Twenty-six consecutive patients with severe hematochezia but negative nasogastric aspiration and sigmoidoscopy were given saline

purges. Emergency diagnostic colonoscopy was performed after stool and clots were cleared by the purge. Effective emergency colonoscopies were performed in 40 patients and bleeding colonic lesions were found in 70%. Telangiectasia or angiomata were the source of bleeding in 35% of the patients and most were located in the cecum or right colon. Seven patients with colonic angiomata and 1 with a sessile colonic polyp were treated as emergencies with Argon laser. Because Argon laser did not require contact with these fragile lesions, it was technically easy to use. For small lesions 6-8 watts was effective and for lesions larger than 1 cm in diameter 8-10 watts was often needed in these patients. Only low flow coaxial CO_2 was used to keep the lightguide clear. On follow-up colonoscopy these lesions healed without rebleeding. There were no complications of emergency colonoscopy or Argon laser treatment. Argon laser photocoagulation in the colon appears to be safe and effective for endoscopically accessible bleeding mucosal lesions.

RESULTS OF OTHER INVESTIGATORS

Bowers and Dixon (16) treated thirteen patients with GI angiomata and recurrent GI bleeding. Two patients had O-W-R syndrome. Associated conditions included aortic stenosis in 46%, renal failure in 23%, arteriosclerosis in 15%, and essential thrombocythemia in 7.5%. Lesions were treated with Argon laser, 3-4.5 watts applied in 1-5 sec pulses. Eleven patients with 105 lesions of the stomach and duodenum and 5 patients with 46 colonic lesions were treated in 22 sessions during the mean follow-up period of 6.2 months. Five patients had angiomata in both the upper and lower GI tracts. In comparisons at 1, 3, and 6 months pre- and post-treatment, the frequency of bleeding episodes and transfusion rates were reduced. There were no complications.

Waitman et al. (17) used an Argon laser at 7.5 watts to treat 50 patients with GI hemorrhage secondary to angiomata. No complications occurred. After treatment, two thirds of the patients had complete cessation of hemorrhage during follow-ups of 6 months to 4 years. One third had decreased GI bleeding and transfusion requirement but required further treatments. One of the 50 patients with GI angiomata required surgery for a bleeding jejunal angiomata.

Rogers (18) reported successful treatment of 50 patients with GI angiomata using a hot biopsy forceps (monopolar electrocoagulation). One patient with a lesion on the ileocecal valve could not be coagulated and required surgery. The distribution of lesions was 44 colonic, 5 gastric, and 2 duodenal. Thrity-nine of the 51 patients (76%) had some type of associated cardiac, vascular, or pulmonary disease. Five patients have been followed for more than 5 years and 2 of these have recurrent GI bleeding and angiomata. No complication were reported.

Young et al. (19) treated multiple gastric O-W-R lesions (average 6/patient) in 3 patients with endoscopic sclerosis. Sodium morrhuate was injected submucosally. Transient bleeding was a complication from two lesions. Endoscopic evaluation at 6 months revealed no telangiectasia and the patients had no recurrent bleeding.

Johnston treated 440 angiomata in 22 patients with a YAG laser. Good outcomes with a reduction or complete control of GI bleeding resulted in 19 patients. Delayed massive hemorrhage 7 to 16 days after YAG laser coagulation occurred in 3 patients (13.6%). Surgical pathology revealed bleeding from induced ulceration at the treatment sites. However, Johnston cautioned that the risk of delayed bleeding should be weighed against the potential benefit of YAG treatment for GI angiomata.

LIMITATIONS OF ENCOSCOPIC COAGULATION AND CONCLUSIONS

Although these techniques are promising, there are several limitations. These techniques are palliative. Follow-up must be empirically determined for each patient. It depends upon the 1) underlying etiology: O-W-R vs non-O-W-R angiomata; 2) the severity and extent of the GI lesions and 3) the severity of concommitant heart failure or valvular heart disease. The benefit to the patient will depend upon careful localization of bleeding sites rather than treatment of non-bleeding angiomata. Patients with circumferential, transmural A-V malformations or extensive, contiguous angiomata are not candidates for endoscopic treatment.

Whether the benefit to the patient of endoscopic treatment of angiomata outweighs the effort, expense and risk has not been previously reported for any coagulation method. Results with Argon

laser are very promising. Studies with other endoscopic coagulation methods are warrented.

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14. NON-GASTROINTESTINAL USES OF LASERS IN MEDICINE AND SURGERY

G. Machicado and D. Jensen

Medical laser therapy first became well established in ophthalmology where Argon laser photocoagulation remains the treatment of choice for diabetic retinopathy. Various lasers are now available for diagnosis and treatment in other specialties of medicine and surgery. The carbon dioxide (CO_2), argon, and neodymium-yttrium-aluminum-garnet (YAG) lasers have significant promise in one or more medical applications (see Table 1).

For any given laser, the principle determinants of its medical applications are the laser-tissue effects, wavelength, lightguide characteristics, power output, cost, size, and portability. All medical therapeutic lasers are expensive. Most are large, heavy, not portable and require special electrical and water outlets. Patients are usually transported to a therapeutic laser unit for treatment rather than moving the laser equipment to the bedside. Multicisciplinary laser centers have been organized in some large hospitals to facilitate laser therapy (see Chapter 15).

Table 1.

	CO_2 laser	Argon	YAG
Ophthalmology	No	Yes	Yes
Dermatology	Yes	Yes	Yes
Gynecology	Yes	Yes	Yes
General surgery	Yes	Yes	Yes
Neurosurgery	Yes	Yes	Yes
Urology	No	Yes	Yes
Enterology	Yes	Yes	Yes
Plastic surgery	Yes	Yes	Yes
Gastroenterology	no	Yes	Yes
Dentistry	Yes	No	Yes
Pulmonary	No	Yes	Yes
Thoracic surgery	No	Yes	Yes

Argon laser light is selectively absorbed by the color red (or hemaglobin) whereas CO_2 or YAG wevelengths are not see Chapter 1). This characteristic makes Argon laser ideal for selective coagulation of vascular abnormalities such as hemangiomata in dermatology or gastroenterology, and diabetic retinopathy in ophthalmology.

The net effect of laser light on tissue is a temperature rise and either coagulation or vaporization. Coagulation is the desired effect for hemostasis and vaporization for ablation (see Chapters 1 and 2).

The depth of tissue penetration and volume of heating or coagulation in increasing order is CO_2 laser (very superficial 0.5 mm), argon (1-2 mm), and YAG (3-4 mm). The time required for treatment with a laser (cutting or coagulation) of a given tissue volume also follows this order. However, the potential tissue destruction effec of a medical laser must be balanced with the need to preserve neigh boring healthy tissue. For example, these differences account for YAG's application to bulky tumors in endoscopy or surgery but the use of CO_2 laser for treatment of decubitus ulcers.

Argon and YAG wavelengths can be efficiently transmitted via flexible quartz lightguides. This characteristic assures easy use of Argon and YAG laser fiberoptic endoscopes in pulmonary or GI medicine and surgery. Lenses can also be used to focus or diverge laser light as necessary for different medical applications. At the present time, there is no practical, safe, and small diameter flexible lightguide for CO_2 laser. Rigid endoscopes, articulating arms, mirrors, lenses, and special non-flexible hand pieces are necessary for CO_2 medical laser applications (see Chapter 15).

In ophthalmology, coagulation of retinal aneurysms and diabetic retinopathy with Argon laser photocoagulation is routine. Other new therapeutic laser applications in ophthalmology for Argon or YAG lasers are the treatment of open angle glaucomam retubak detachment and opacified lenses.

In dermatology or plastic surgery, Argon, CO_2, and YAG lasers are all being applied. Techniques and guidelines are empirical at this time. With a variety of hand pieces for focusing or divergence of laser light, Argon laser is reporte to give excellent results for treatment of cutaneous portwine stains, telangiectasia, keloids tattoos, and spider angiomata (1). When Argon laser can not control

the cutaneous vascular lesions, YAG has been applied in some treatment centers. However, because of the deeper depth of penetration, there is an increased risk of burning and scarring. On the other hand, Kaplan et al. (2) reported good results with CO_2 laser treatment of 552 patients with dermatologic conditions. Lesions treated were nevi, hemangiomata, telangiectasia, pyogenic granuloma, papillomatosis, senile keratosis, warts, xanthelasma, tattoos, superficial and basal cell carcinomas. The results of Argon, CO_2, and YAG lasers for different dermatologic conditions have not been compared under similar conditions. Therefore, which laser is best for certain dermatologic treatments has not been determined.

In gynecolology, CO_2 and YAG lasers have been applied. In separate series Baggish (3) and Belina (4) treated infertile womin with CO_2 laser microsurgery and reported goods results. Intraoperative CO_2 laser treamtnet of endometriosis and adhesions have been performed successfully. Recently, Fuller and Goldrath (5) treated menorrhagia in 120 patients with YAG laser. There were excellent results, no complications, and hysterectomy for hemostasis was avoided in most patients.

In urology, partial nephrectomies can be performed with CO_2 lasers. Barzilay and Fine initially performed nephrectomies in dogs and later applied the technique successfully to six patients at surgery (6). YAG and Argon laser have been applied via flexible lightguides through cystoscopes for treatment of a variety of bladder lesions including tumors, papillomas, and stones (7). Other urologic applications of medical lasers and for treatment of penile tumors, condyloma acuminata, hemangiomata, and circumcision.

In general surgery, Argon, CO_2 and YAG lasers have been applied. Some studies suggest that lasers may have some advantages over routine surgery under certain circumstances. For example, the CO_2 laser is very effective for debridement of decubitus ulcers with improved healing compared to routine medical-surgical management. Both Argon and YAG lasers can be applied with a laser scalpel that allows mechanical cutting with a quartz blade and simulatneous laser photocoagulation (8). Partial hepatectomies, splenectomies, and hepatic tumor resections are amendable to such treatment. Hemorrhoidectomies, fistulectomies, excision of anal fissures, pilonidal cysts, and anal tumors have also been successfuly performed with decreased

post-operative pain, excellent hemostasis, and less post-operative complications than with routine surgery. Giler reporterd good post-operative healing after CO_2 laser excision of cutaneous tumors and subsequent primary closure, split thickness skin grafts and rotatio. flaps (2).

Laser are being applied in neurosurgery for excision of lesions (CO_2, YAG and Argon (9)) and repairing severed peripheral nerves (argon). W. Scheiblbrandner reported a reduction in post-operative complications in the treatment of carpal tunnel syndrome with the use of a CO_2 laser as compared retrospectively to routine surgery (10). W. Taki used a YAG laser to resect pituitary adenomas, meningiomas, gliomas, an AVM, and other tumors. Very effective coagulation with YAG laser and easy maneuverability with the flexible lightguide were definite advantages of YAG laser in neurosurgery particularly where the surgical field was limited.

In thoracic surgery and pulmonary medicine, the YAG laser has been life saving for some inoperable patients with obstructing tracheobronchial tumors. Both flexible and rigid bronchoscopes have been used during treatments with good results. With successful endoscopic treatment, thorachotomy can be obviated for some patients. However, vaporization of obstructing endobronchial tumors carries a risk of perforation or fatal hemorrhage from erosion into a major artery. In Europe, Dumon (11) and others are treating many patients with both bening and malignant endobronchial tumors with endoscopic YAG laser. In the United States, Cortese (12) and others are primarily treating malignant lesions in high risk patients because of the potential risks of the procedure.

Lasers have been studied in the prevention and treatment of dental carries. It has been reported that laser energy will change the tooth crystalline ultrastructure, making it more resistent to bacterial or acid decay (13).

Other applications of lasers are for diagnosis and treatment of malignancy. Selective absorption of certain laser wavelengths by dyes or hematoporphyrin derivatives can be used for tumor detection with low power photoactivation of intracellular dyes and oncolysis. For example, after hematoporphyrin injection, subclinical endobronchial tumor detection via bronchoscopy is possible with low power Argon laser photoactivation.

As more basic and clinical studies emerge, lasers will find their niche in clincial medicine. Ongoing investigation, technological advances, and further research surely will open the doors into unforeseen therapeutic applications.

In view of the multiple uses for lasers in medicine and surgery now, multispecialty laser units have already been formed and are successfully coordinating treatments. A multidisciplinary approach appears very rational because of the cost, non-portability, and maintenance requirements of currently available medical lasers.

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15. ORGANIZATION OF A MULTIDISCIPLINARY LASER CENTER

J. M. Brunetaud, L. Mosquet, J. Bourez and A. M. Wierez

There are laser therapeutic applications in many medical fields. Three different lasers are generally used: carbon dioxide (CO_2), argon ion, and Nd YAG. Often one laser does not allow a specialist to treat all his cases. He may need either argon and Nd YAG for gastroenterology and urology; argon and CO_2 for dermatology or plastic surgery; CO_2 and Nd YAG for general surgery or neurosurgery. The cost of these machines prohibits any one specialist from having several lasers. It is more practical to group medical lasers in a department specializing in laser treatment. Furthermore, physicians and surgeons will meet together, discuss techniques, and be able to choose the best laser for each indication.

DESCRIPTION OF OUR LASER CENTER

The lasers

At present we have the CO_2, Argon and Nd YAG lasers.

The CO_2 (CM 500 CILAS-Biophysic Medical) has a TEM 00 emission with a maximum output power of 50 watts continuous wave (CW), or 350 watts pulsed at 500 Hz. The Nd YAG laser (YAG Medical 100 CILAS-Biophysic Medical) has a maximal output power depending on exposure time: 50 watts CW to 120 watts at 0.25 seconds. (It should be noted that the American and German GI YAG lasers are water cooled and not as portable.) These two French lasers have a water-air cooling exchange; they only require electric and gas connections. They can easily be moved from one room to another situated at the same floor.

The Argon laser (770 Cooper - AHS) has a maximum output power of 10 watts CW. It is a fixed unit because of the water connection for cooling and the special voltage (208 volt) different from the European standards (a special transformer is required).

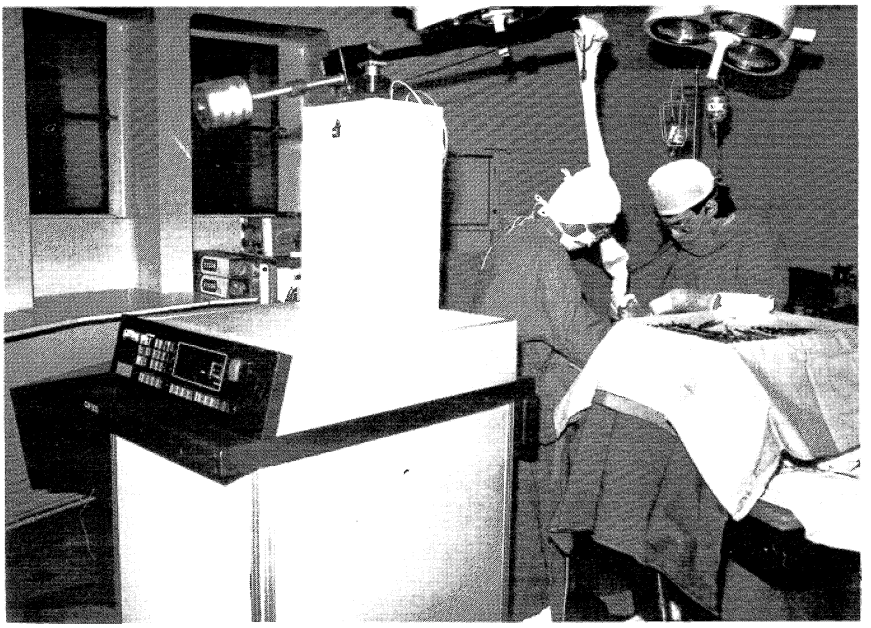


Figure 1. CO_2 laser and surgery unit

Figure 2. YAG laser application for colonic tumor ablation (Gastroenterology)

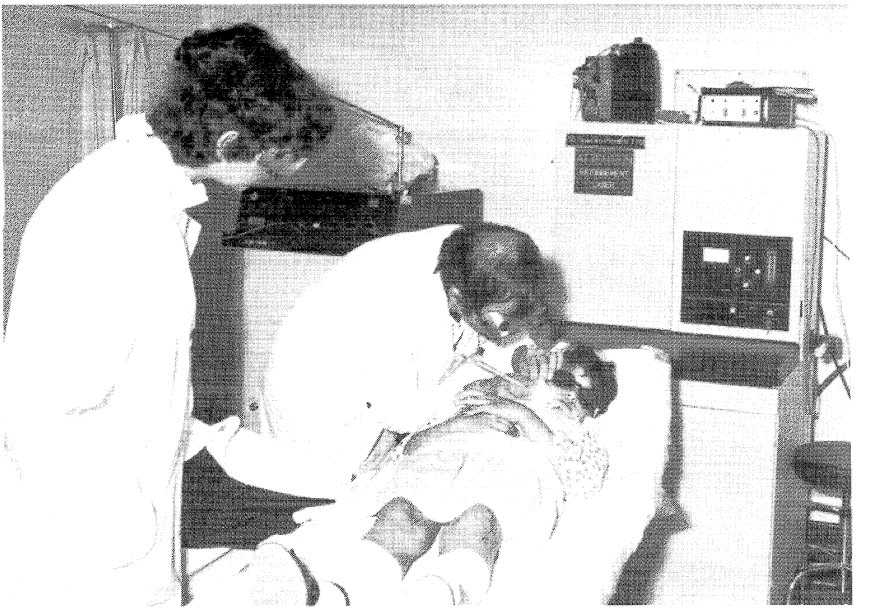


Figure 3. Argon laser treatment of a hemangioma (Dermatology)

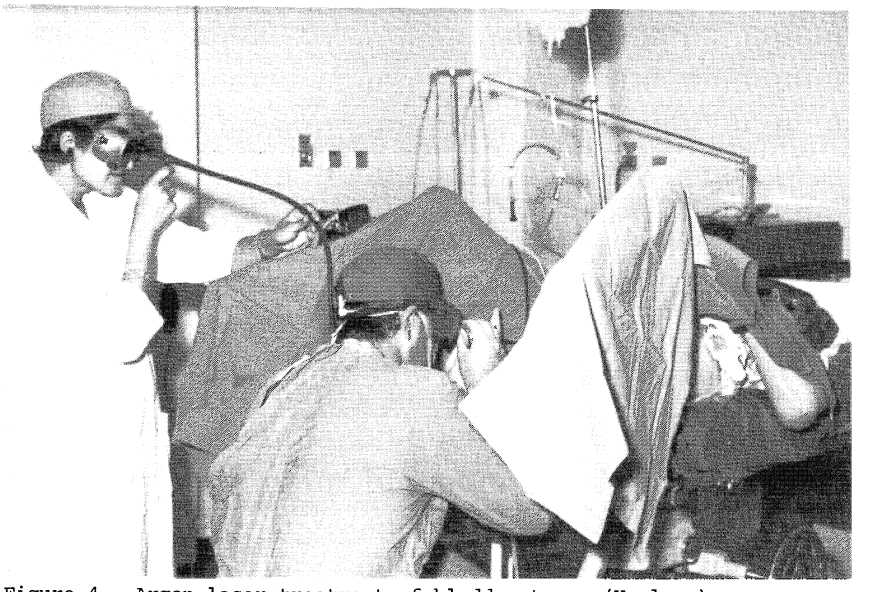


Figure 4. Argon laser treatment of bladder tumor (Urology)

Optic fibers for argon and Nd YAG are special products manufactured at LILLI (SOMIMECAR). Different endoscopic laser probes and hand-piedes are adapted to each medical application (see Chapter 14).

For external use (dermatology, gynecology) the handpieces are equiped with 3 different lenses easily changeable without adjustments. Three spot sizes are available: 0.2, 0.6, and 1.2 mm for argon and 0.4, 1, and 2 mm for Nd YAG.

For digestive endoscopy, Argon and Nd YAC laser probes have 1.7 mm external diameter (compared to the 2.2 mm of commercial products). These thin laser probes are also very useful in bronchoscopy For urology a special system has been designed to replace the gas insufflated into the probe by water via a non-modified cystoscope.

All the routine maintenance of the lasers and fibers is performed by the laser unit personnel.

The laser room

We have two different laser rooms: one for surgery with the CO_2 laser and one for endoscopy and dermatology with Argon and Nd YAG. They are located at the same floor, at a distance of 50 meters. Both have facilities for general anesthesia and resuscitation. An air conditioning system operates in the endoscopic room. In the surgical room the smoke is eliminated by aspiration. A recovery room, a waiting room, a secretary and an office are included in the laser center.

The staff

According to the central philosophy established by the laser center director, each physician or surgeon comes to the center with an assistant to treat his patients. The permanent staff of the lase center assists them as necessary. The staff of the laser center is composed of 4 nurses, 1 secretary, and 3 medical doctors: a resident, an anesthesiologist, and the chief of the department.

LASER CENTER ORGANIZATION

Each specialist has reserved time in the laser center schedule. Cases are scheduled the week before. In case of vacancy or cancel-

lation, the time slot is given to any doctor with other cases. The 4 main users are gastroenterology (5 half days), plastic surgery (4 half days), dermatology (3 half days), and gynecology (2 half days).

Urologists, general surgeons, dentists, oral surgeons use the center at least once a week. Other specialties had their own lasers before the opening of the specialized laser center: opthamology (2 Argon lasers), ENT (a 20 watts CO_2 laser) and pneumology (a YAG laser). They are in a close contact with the center for technical problems and they sometimes come for special indications. Examples are endoscopic coagulation for the pneumologist, argon nares coagulation or high power CO_2 surgery for ENT surgeon.

CONNECTION WITH THE LILLE MEDICAL LASER RESEARCH CENTER (CERLAM)

The clinical work carried out at the Regional Hospital is only one aspect of the CERLAM activity. In collaboration with engineers of the Sciences University and the Medical Research Institute, we design new systems (optic fibers, high power CO_2 wave guide laser) and test them on animal models at the experimental laboratory of the Medical School. A modified thermo camera (AGA-Sweden) allows a very precise study of laser thermal effects on tissue. Most of the physicians and surgeons using the lasers at the hospital have first learned the laser technique at the experimental laboratory.

DISCUSSION

The Lille laser activity was started in a single room with an Argon laser 1978, an Nd laser was added in 1980 and a CO_2 laser in May 1982. At this time all the rooms described above are fully functional. The Lille laser center with the 3 lasers has been working for only 6 months, but is fulfilling its purposes:

A. Many specialties would not have started any laser activity without the center. At present, 10 of them are currently using its facilities.

B. The overall occupation of the 2 laser rooms is about 80% which gives time for the maintenance. No treatment interruptions have occurred because of technical failure.

C. All practitioners follow the same method for collecting dat in order to evaluate the efficacy and safety of the treatments.

There is actually a tendency in France to open such centers ir the main hospitals. At present only Toulouse Hospital has a 3 las department. But several hospitals have 2 lasers (Argon and Nd YAC Nd YAG and CO_2) and will buy the third soon. Exchange of data between centers is frequent and allows a better utilization of th lasers for medical treatments.

16. COMPLICATIONS OF ENDOSCOPIC LASER THERAPY

J. Johnston

It was with some trepidation in 1979 that this author entered clinical laser work in a community hospital setting. A YAG laser was chosen because of its apparent superior hemostatic efficacy, but there were some reservations regarding its safety. Our extensive animal studies had revealed full thickness gastric wall damage with this laser, despite attempts to modify multiple treatment variables (1). This potential for thermal injury with the YAG laser was similar in quantity to monopolar electrocoagulation, but greater than that seen with either argon laser or bipolar electrocoagulation (2). Although a relatively low perforation rate of 2% had been noted by Kiefhaber, systematic human pathologic study had not been reported (3). Therefore, with the inauguration of my clinical laser work, a commitment was made to actively search for any possible complications and report them (4). Routine post-treatment radiographs were obtained to look for free or loculated intraperitoneal air. No patients were simply treated and then returned to another physician for followup. With patients who were sent to surgery, there was close inspection of the treatment site for serosal whitening or evidence of perforation. Autopsy was obtained whenever possible on patients who died for any reason, and careful gross and microscopic examination of the treatment site was performed.

Complications following a variety of endoscopic thermal modalities are similar. One might anticipate complications related to the endoscopy itself, the coaxial gas jet, or thermal injury (Table 1).

Endoscopic complications occur up to ten times more frequently

with emergency endoscopy for UGI bleeding than with routine endoscopy (5). Perforation due to instrumentation may occur with a difficult emergency endoscopy. Aspiration of blood and gastric contents may be a hazard unless adequate safeguards are taken. Endotracheal intubation should be considered in situations where aspiration is likely. Examples include massive variceal hemorrhage, the use of large tube gastric lavage, and rolling patients in various positions during the endoscopy (especially with the right lateral decubitus position, in which the fundic pouch is emptied and the esophagus may be dependent). Therapeutic endoscopists infrequently report aspiration as a complication; however, its incidence may be underestimated.

A traumatic endoscopy may induce active bleeding, especially from esophageal varices (5). A bleeding Mallory-Weiss tear may result from wretching associated with endoscopy. Gastric lavage or endoscopy may induce abrasions or suction artifacts which may be falsely identified as the true bleeding point. In one patient who had a non-bleeding antral ulcer on initial endoscopy, I noted active arterial pumping from the ulcer following large tube lavage to remove fundic clots. Vigorous washing, irrigation and suction of overlying blood clots to allow close inspection of the ulcer bed and target vessel may increase or induce bleeding. Although Storey, et al. reported that the target site could be cleansed without exacerbation of bleeding, this needs to be confirmed (6). Additionally, the prolonged nature of many therapeutic endoscopic procedures may increase the risk of complications.

Regarding thermal complications, tissue damage, necrosis and ulceration are produced by heat regardless of the modality used. Small ulcerations of normal mucosa in the UGI tract usually heal over in one to two weeks, but take longer in the colon (personal communication, D. Jensen). Prolonged ulceration may rarely be seen, as with malnourished patients with impaired tissue healing (personal communication, R. Dwyer). The depth of histologic injury is significantly greater with the YAG laser or monopolar electrocoagulation compared to the argon

laser, bipolar electrocoagulation and the heater probe (2). With submucosal and muscle layer injury, destruction of cells is common, although the collagen matrix remains and gives some strength to the damaged wall. This may account for the lack of perforation seen after surgical use of electrocautery which often produces full thickness tissue injury.

Tissue components react differently to heat, although this has not been studied in a comprehensive manner. Using thermal coagulation, Dixon reported that canine gastric serosa retains its integrity longer than the muscle layer, and he suggested that the serosa may be an important barrier preventing perforation (7). Animal experiments to assess the tensile strength of the various gastrointestinal tract layers following different thermal treatments would be of considerable interest.

The longer tissue is heated, the greater the chance for perforation. However, most clinical investigators do not define a ceiling or upper limit on the total energy which may be applied safely during treatment. It is recognized that caution should be exercised in areas of the gastrointestinal tract which have thin walls, such as the cecum (especially thin) and esophagus (no protective serosa), but also the small intestine and other parts of the colon. Additionally, the target wall may be relatively thin in settings such as acute stress ulceration, advanced age, and especially with endoscopic overdistention. Fortunately, with the endoscopic thermal modalities used to date, there appears to be an acceptable margin of safety, and there are few "surprises".

The major "surprise" is vaporization. With a small laser spot size at a short treatment distance, excessive power density may produce surface temperature elevation to 100°C which causes vaporization or acute ablation of tissue. Indeed, just as electrocautery or the carbon dioxide laser can be used as a surgical scalpel, the argon or YAG lasers may produce the same cutting effect. This property is utilized in endoscopic ablation of tumors, but is distinctly undesirable with photocoagulation of gastrointestinal bleeding lesions. In the laboratory using

a canine model, the thick gastric wall can be perforated with only a few seconds of laser application at high power density (7). Similarly, in our early experiments using endoscopic argon laser, pinpoint perforations were noted occasionally when treatment efficacy was poor and treatment distance was shortened in order to intensify heating of the tissue. It is also possible to erode large submucosal vessels, inducing massive arterial bleeding (8). Undesirable erosive effects may be more likely with the argon laser because of its superficial absorption and close treatment range. Although an erosive effect with the YAG laser clearly is a potential hazard also, the range of treatment distance is not as restricted with YAG, and deeper penetration of this wavelength avoids the preferential superficial heat deposition seen with the argon laser and especially with the carbon dioxide laser. Because of the potential for tissue vaporization and induction of hemorrhage, caution is necessary with any thermal treatment of visible vessels or large angiomata. After experience with argon or YAG laser, visible erosive effects can be recognized during endoscopic treatment, in which case power density should be reduced by increasing treatment distance and/or decreasing power.

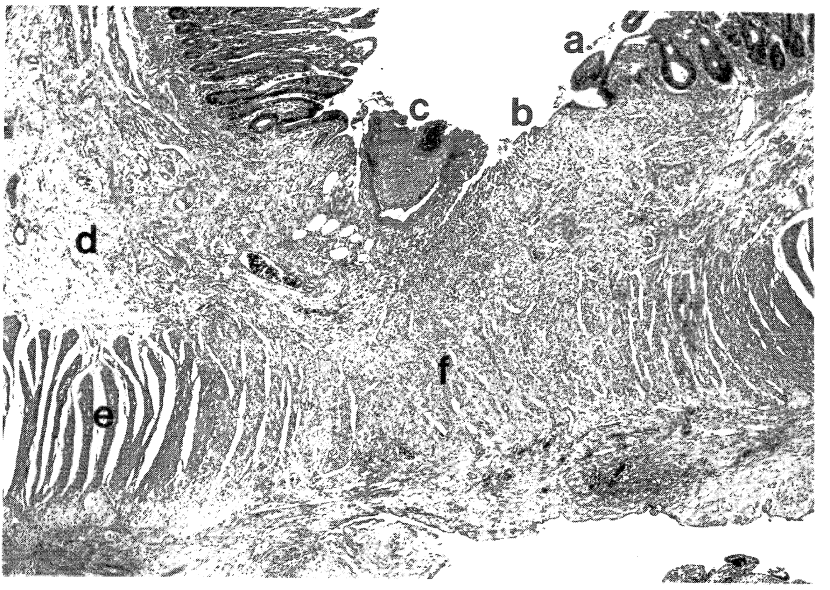
Maximal tissue injury recognizable by light microscopy occurs 3 to 7 days after thermal treatment. At that time, nonviable tissue may slough, producing deeper ulceration. There is a potential for delayed perforation at this time, as well as secondary bleeding. This phenomenon is also well recognized following colonoscopic polypectomy with monopolar electrocautery snares (9).

The incidence of recognized UGI perforation has been 1% to 2% for reported YAG clinical series (3,10), 0% for argon (11), and 0% to 2% for monopolar electrocoagulation (12,13). In my own clinical experience with 100 YAG treatments, there was one definite perforation due to thermal injury of the mid esophagus (14). This inoperable patient exsanguinating from an esophageal varix required a prolonged treatment with 8,000 joules for hemostasis. In retrospect, there was probably some

additional difficulty due to vaporization with a close tangential treatment. Kiefhaber noted that his perforations occurred primarily in the setting of acute stress ulceration (3). Most reported perforations were delayed, occurring 2 to 5 days after the thermal treatment.

Initiation or exacerbation of hemorrhage with thermal treatment can occur by disruption of a fragile clot, erosion into a vessel, vasodilation, or coagulation of the artery distal to the bleeding site. In my series of 47 cases of active GI hemorrhage treated with the YAG laser, 8 had significant exacerbation of brisk or arterial bleeding during laser treatment; however, all but one were controlled with further laser therapy (14). For 9 patients treated with non-bleeding visible vessels in ulcers, 4 had induction of arterial bleeding; 3 of these could not be controlled with the laser and 2 required immediate surgery. Swain reported that in 2 of 17 patients with non-bleeding visible vessels, the argon laser caused uncontrollable hemorrhage that required immediate surgery (15). Rutgeerts reported that YAG laser exacerbated bleeding in 20% of patients (16). In the United States, there has been one death related to YAG laser-induced uncontrolled hemorrhage from a large duodenal ulcer with visible vessel in an inoperable patient. It is expected that this potential is common to all thermal modalities, and anticipation of this complication should deter the endoscopist from initiating treatment under less than ideal conditions, from using a modality of questionable hemostatic effectiveness, or from treating visible vessels when surgical backup is not available. This complication also makes one question whether or not all non-bleeding visible vessels should receive endoscopic coagulation therapy, since up to 50% of such patients will not rebleed or require surgery (6).

In my series, delayed hemorrhage of a massive nature (mean of 9 units) followed YAG laser treatment of angiodysplasia in three instances (total of 440 lesions coagulated in 22 patients) (4). In each instance, low energy was employed with the laser treatment. In two of the cases, surgical pathology



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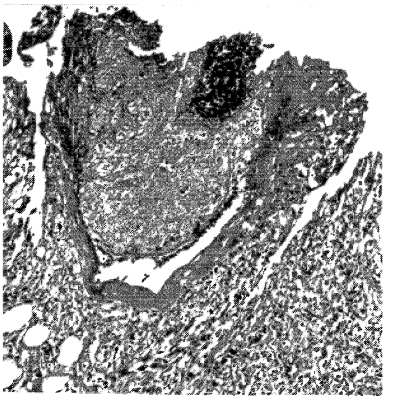

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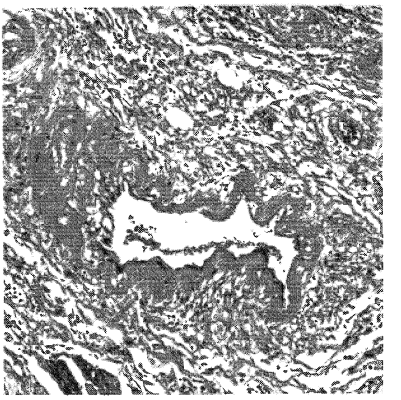


C

Table 1. Complications of Endoscopic Coagulation

I. Nonthermal

A. Endoscopic

- Perforation
- Aspiration
- Induced hemorrhage
- Medication reaction
- Hypotension
- Arrhythmia

B. Coaxial gas jet

- Overdistention
- Air embolism
- CO_2 retention
- Pneumatosis, benign pneumoperitoneum

II. Thermal

A. Acute

- Exacerbation of bleeding
- Ulceration
- Perforation
- Edema, obstruction

B. Chronic

- Delay in healing
- Perforation
- Stricture
- Delayed hemorrhage
- Infection

Legend (Figure 1).

A. Histologic section of jejunum (magnification x 40) from a patient who bled massively 8 days following YAG laser coagulation of multiple small bowel angiomata. Jejunal bleeding source was found at surgery to be laser-induced ulceration with exposed artery in ulcer base with adherent clot (separated during histologic processing). Note full thickness damage to intestinal wall, despite low energy application. (a - mucosa, b - ulcer, c - exposed vessel, d - submucosa, e - muscularis externa, f - laser-induced transmural damage).

B. Magnified view (100X) of laser-damaged artery described in A.

C. Same artery as B traced in serial sections back to area not treated with laser, demonstrating normal arterial appearance (100X).

revealed arterial bleeding from ulceration at a treatment site (Figure 1). In one of these cases, the laser damaged submucosal artery could be traced back to sections that did not contain angiomatous tissue. A normal artery was probably damaged by the laser treatment and bled massively when tissue slough occurred at seven days. In the third case, a patient bled massively from laser induced gastric ulceration 16 days later, but was successfully coagulated with further laser therapy. Bown also recalled a patient with arterial bleeding two days following argon laser treatment of a gastric telangiectasia (personal communication, S. Bown). With monopolar electrocoagulation of angiodysplasia, Weaver noted several instances of delayed bleeding from iatrogenic ulceration (17). This type of delayed hemorrhage following all forms of thermal coagulation is due to tissue slough and ulceration of normal arterial wall injured by heat. The phenomenon is most easily recognized in angiodysplasia patients who have oozed but never bled massively. It is suspected, however, that some of the "rebleeding" seen after coagulation of bleeding ulcers may actually represent this same problem. This may be reflected in Swain's controlled trial by rebleeding in 3 of 12 argon laser treated patients with stigmata of recent hemorrhage without visible vessels, whereas 0 of 12 control patients rebled (15). Further information from controlled trials may help define the potential incidence of this complication. It is anticipated that this problem would occur less often with more superficial thermal modalities (argon laser, bipolar electrocoagulation, heater probe) as compared to deeper ones (YAG, monopolar electrocoagulation).

A minor complication of thermal coagulation relates to the tissue edema produced. Following successful YAG laser coagulation of a bleeding pyloric channel ulcer, one of my patients experienced transient gastric outlet obstruction which was successfully managed with nasogastric suction for two days. In an analogous situation, Fleischer, in his work ablating esophageal malignancy, has noted transient exacerbation of esophageal obstruction that resolves within 1 to 2 days (personal communi-

cation, D. Fleischer).

The last category of complications is related to the coaxial gas jet used with the laser (Table 1). Although venting and recycling systems are available, there remains a real hazard of bowel overdistention. With the YAG laser, at least 10 cc/sec is recommended to protect the waveguide tip from contamination, and up to 60 cc/sec is often used with endoscopic laser application to clear overlying blood. With the argon laser, use of an effective coaxial gas jet is much more important for treatment of bleeding lesions, and gas flow of 80 cc/sec is often employed for active bleeding. These figures translate to 36, 216, and 288 liters of gas respectively introduced into the target organ during a one hour treatment session! The potential for inadvertent overdistension is obvious.

If a thermal treatment is applied to an overdistended, thinned out target wall, the incidence of deep tissue damage is greatly increased (8). Although effective recycling of the coaxial gas is helpful, there is no device available to accurately monitor endoscopic distension. Pressure probes are not helpful because a distensible hollow viscus can stretch notably before a significant pressure rise occurs. The most useful way to avoid overdistension is to consider this possibility frequently during a treatment, to use manual suction freely, and to avoid visual effacement of mucosal folds.

If the coaxial gas is room air, there is a theoretical concern regarding air embolism, although this has not been reported with endoscopic laser therapy. To avoid this potential hazard and to allow more rapid absorption of the gas, carbon dioxide is often preferred to compressed air. CO_2 absorption and hypercarbia may become significant in patients with chronic obstructive pulmonary disease and impaired CO_2 exchange.

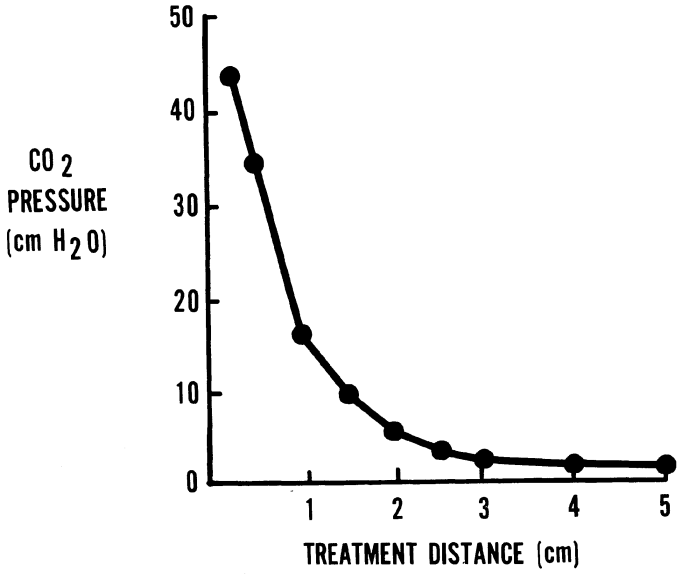
Another problem related to the coaxial gas jet is gas dissection through the target wall, producing pneumatosis and/or a benign pneumoperitoneum. In my series of 100 YAG laser treatments, there were three instances of pneumoperitoneum found on routine posttreatment xrays (4). In two of these cases,

contrast xrays revealed no leakage, and there was no abdominal pain, tenderness, ileus, fever, leukocytosis or other untoward effect. In the third case, pneumoperitoneum followed a low energy treatment of cecal angiodysplasia. The surgical specimen revealed prominent retroperitoneal and cecal subserosal pneumatosis and no free perforation, although peritoneal culture grew Escherichia coli in very low titer. Upon filling the resected right colon with water, no leakage of fluid occurred. It is felt that this regional subserosal emphysema represented a dissection of high pressure CO_2 gas through a laser induced mucosal erosion, with subsequent rupture of a gas-filled bleb. Dixon, in canine experiments using the argon laser with coaxial CO_2, also observed occasional dissection of gas between layers of the colon, extending into the adjacent mesentery (18). As shown in Figure 2, there is an exponential rise in the force of the CO_2 gas jet at close treatment distances and an extremely high pressure results when the CO_2 catheter inadvertently touches the target mucosa. This type of dissecting microperforation and gas leak should be distinguished from a free direct thermal perforation discussed earlier. A similar benign pneumoperitoneum has been described following other endoscopic procedures and can be treated conservatively if appropriately recognized (19).

Concomitant use of a high flow coaxial gas jet or water jet irrigation is essential for effectiveness with the argon laser in treating actively bleeding lesions. In contrast, the YAG laser may be used effectively without a coaxial gas jet. With the YAG laser, I now prefer to use occasional bursts of coaxial gas to clear debris from the fiber tip, rather than employ constant gas flow.

In summary, in addition to a risk of perforation from excessive thermal energy, the therapeutic endoscopist should be aware of tissue and vessel erosion produced by excessive power density; the hazards of overdistension, dissecting microperforation and gas leak with the coaxial gas jet; as well as delayed massive hemorrhage due to tissue slough following thermal coagulation.

Figure 2. Relationship between CO_2 pressure and treatment distance.



Marked increase in CO_2 back pressure with decreasing distance of coaxial gas catheter from the mucosa.

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17. USE OF LASERS IN COMMUNITY HOSPITALS IN THE UNITED STATES

B. Overholt

The use of lasers in gastroenterology has been pioneered by a small but increasing number of gastroenterologists and surgeons. Their efforts have effectively captured the interests of others who recognize the potential for laser use in the community hospital for patients with digestive diseases. The acquisition, implementation, and utilization of GI lasers raises a number of interesting issues which this presentation attempts to address.

WHAT IS REQUIRED (Table 1)

A decision to embark on developing a laser service in a community hospital requires considerable forethought as such a decision requires a significant investment in time and energy from the physician and the hospital. The physician must dedicate time not only for education preparation but for negotiations with the hospital and other physicians. Adequate facilities including space, plumbing and electrical wiring are necessary. The hospital must commit to purchase the equipment which is more than a minor budgetary item. Training is necessary for the physician – endoscopist and equally important, the endoscopic assistant team, which will be primarily a responsibility for the physician. Protocol development is an absolute as gastrointestinal (GI) laser are classified by the Food and Drug Administration (FDA) as investigational at this time. Although master protocols are available, modifications to fulfill and meet local requirements are necessary. Protocols must then be submitted for the hospital human use committee approval, followed by a submission to the FDA for investigator-protocol approval.

Table 1. GI laser – what's required.

Physician decision
Adequate facilities
Commitment purchase
Training
Protocol development
Hospital human use approval
FDA approval

LASER-CRITERIA FOR USE

Which physicians use the laser should and must be carefully controlled to ascertain proper utilization in the fullest and best meaning of the term "proper utilization". This necessitates that the physician have:

1. Endoscopic privileges
2. Proper training
3. An approved protocol
4. Hospital human use committee approval
5. FDA approval
6. Proper facilities
7. Trained endoscopic assistants.

Training is essential. With a background of endoscopic competence, the best training for the endoscopist is a combination of didactic instruction, hands-on experience in a dog lag with laser use, followed by direct supervision of an endoscopist skilled in GI lase. use, if available. An alternate route would be the combination of didactic instruction, observation of procedures being done by a skilled endoscopist using the laser, followed by intense and direct supervision of laser use until the trainee be judged competent. These criteria should be adopted by all facilities embarking on the development of a GI laser service.

LASER – HOSPITAL VIEWPOINT

The hospital has its concerns that must be addressed. Not only is quality of care a concern, but costs are being given increasing attention in a time of hospital budgetary constraints. More relevance is being given to this statement since, at least initally,

the laser service is one that likely will not pay its own way. Facilities must be made available. Personnel must be trained and available – preferably 24 hours a day. Charges for laser use must be determined. Potential utilization by other physician and other medical and surgical specialists is an important consideration. The hospital must have the physician commitment to "make it go". These are areas the physician should be prepared to discuss with the hospital when approaching the administration about a laser service.

ACCEPTANCE BY THE PHYSICIAN COMMUNITY

Peer acceptance is a key element if a laser service is to succeed. This requires groundwork to be lain with physician leaders in the hospital and with referring physicians. Education of these physicians is essential. Additionally the concept of a multi-disciplinary laser suite is one to be used in discussion with physicians and the hospital to promote the laser program. If several subspecialty physicians can use the same laser, then the hospital administrators will likely be more recepttive.

Urologists, dermatologists, bronchoscopists, and gynecologists may all benefit GI lasers (Nd YAG, Argon) and their support should be solicited. Lasers are and will change much of what we do in medicine, and physician leaders who recognize this should be enjoined to support lasers.

LASER PREPARATION: EQUIPMENT/DRUGS (Table 2)

Although the treatment technique for the endoscopic laser therapy of GI bleeding is covered in another section of this text (Chapter 7), the authors guidelines will be reviewed here as they apply to the community hospital setting.

Preparation prior to laser use is essential as laser work in UGI hemorrhage is exacting work. Equipment and drugs must be immediately available for use. One must anticipate and prepare for (1) the most difficult situation – the massive bleeder and (2) the worst complication – laser induced massive arterial bleeding (Table 2).

A Monoject or large bore tube is used for thorough lavage of the stomach. Pitressin is available for intravenous use if uncon-

Table 2. Laser preparation: equipment/drugs.

Large bore irrigation tube (Monoject, etc.)	Water pik or syringe irrigator
Pitressin	Blood pump
2 Channel scope (white tip)	Cardiac monitor
Nasogastric tube taped onto scope	Pulse/BP monitor
Snare	Prove insertor needle
William's "Overtube"	Crash Cart
	Photography/TV

trollable bleeding occurs to hopefully reduce the bleeding rate. A two-channel scope is preferred. The white tip can be obtained from one manufacturer to reduce heating and damage to the instrument tip. An NG tube can be taped alongside the instrument for recycling of air/gas in order to allow one channel to be free for other uses. A snare should be available to transect or remove large clots, particularly those in the fundus. The William's tube used in sclerotherapy is useful when inserted to serve as a splint to allow frequent, rapid and safe removal of the scope and clots followed by reinsertion. The tube also protects the patient's airway. The device is inserted over a Maloney dilator passed through the William's tube the dilator removed and the tube is left in place as a splint. The side window is covered with tape to prevent mucosa from protruding into the tube lumen. The use of this technique must be with caution if a large hiatal hernia or esophageal strciture is present and a quick endoscopic survey of the esophagus and stomach is advisable as a first step prior to introduction of the splint.

A water pik or syringe irrigator is needed to remove clots. A blood pump is necessary to allow rapid blood infusion when needed. Cardiac, pulse and blood pressure monitors are advisable to assist in patient monitoring. The commercially available probe insertor needle is helpful in allowing easy non-traumatic passage of the laser probe through the diaphragm guarding the channel portals. A crash cart is essential when and if needed. Photograph and TV equipment is helpful for documentation.

LASER PREPARATION: Personnel

Competent nurse endoscopic assistants are essential. A minimum of two trained assistants should be available with one being on call at all times. With such personnel errors can be minimized. These persons should be carefully trained and prepared for laser work. Teamwork is essential and rehearsal is necessary prior to beginning laser work and at periodic intervals if time between laser uses is excessive. The nurse should not only be capable of setting up for the laser, participating in its use, monitoring the patient but also should alert the operating suite of a potential emergent surgical need for treatment of a massive UGI hemorrhage. Competent, trained nurse endoscopic assistants are mandatory for a successful laser treatment facility.

LASER PREPARATION: PHYSICIAN

The endoscopist using lasers in the treatment of massive UGI hemorrhage should always have a surgeon immediately available. The endoscopist should be prepared to expend 1.5-2 hours or more for active bleeding cases, requiring considerable schedule flexibility. Treatment of visible vessels or spots may require less time but to "sandwich" a laser case into a busy schedule without allowing adequate time is to invite disaster. Training and other requirements for physicians has been dealt with earlier in this text.

LASER PREPARATION: PATIENT

The endoscopist should anticipate the use of the laser and should discuss its potential use with the patient and family including alternatives, risks and complications. Consent forms should be obtained in advance in case the laser is needed. Intravenous lines should be in place – preferably two lines with 18 guage needles. Oxygen administration is advisable particularly in the elderly patient as hypertension and low blood volumes are common in these patients. If possible coagulation defects should be corrected. Blood should be immediately available; four units typed, crossed and available on demand is recommended.

LASER PREPARATION: LASER

Preparation of the laser equipment should be automatic and should be checked by the nurse and the physician. The physician must be thoroughly familiar with the equipment. Room signs should be on outsite doors when the laser is in use. The endoscopisst may use protective goggles, or when the laser is inserted may rely on the protective ocular lens cover. The water cooling system must be on. The power emission from the laser probe should be checked in those machines equipped with this feature prior to insertion. Firing the laser once on normal gastric mucosa to ascertain the "in vivo" tissue effect is another wya to ascertain adequate energy emission before treatment of ableeding site.

LASER PROCEDURE

Again, anticipate the need for the laser and be prepared for its use. Thorough irrigation of the stomach is vital. A diagnostic EGD is performed. An exact diagnosis is absolutely essential as laser application should be precise. The area should be cleared — not only the stmach but the endoscopic room. The endoscopist must be able to give total and absolute concentration to the patient at all times. Observers and assistants likewise should be giving equal attention to the patient. Unnecessary talking, etc. is distracting and should not be tolerated.

SUMMARY

From inception to completion, the planning, development and implementation of a laser service in gastroenterology is a complex procedure requiring maximum commitment of the physician, nursing personnel and the hospital. Guidelines and recommendations from beginning to completion and utilization are presented in detail.

18. LEGAL ASPECTS OF LASER USE IN THE UNITED STATES

C. E. Enderby

The United States federal government first became involved in drug regulations in 1906 with the passage of the Food and Drug Act. This act dealt with misbranding and adulteration. In 1938 the act was expanded to include food and cosmetics. The Federal Food, Drug and Cosmetic Act is the basic food and drug law of the United States, and is the most extensive law of its kind in the world. It is the duty of the Food and Drug Administration to enforce these laws.

In 1962 the act of 1938 was amended. This amendment prohibits distribution of any drug unless approved by the FDA. Premarketing approvals given are based on scientific data provided by manufacturers and are subject to review and acceptance by FDA scientists for safety and effectiveness.

Enactment of the "Medical Device Amendment of 1976" presents the most significant revision of the Federal Food, Drug and Cosmetic Act. The 1976 law brought devices intended for human use under FDA jurisdiction. Generally, the law defines devices as any health care product that does not achieve any of its intended purposes by chemical action, in or on the body, or by being metabolized. New authority to assure safe and effective devices resulted from the amendment.

The 1976 law put devices into three catagories. Class I devices are those for which general controls are sufficient to provide reasonable assurance of safety and effectiveness. Class II devices are those which require a higher degree of control. These devices must adhere to a performance standards for that device. Class III devices are those which require premarket approval because of their lifesustaining nature or because of some possible risk of illness injury, or because they are new types of devices. Most lasers systems are in Class II or III. Argon lasers for ophthalmology use are Class II devices. The Nd:YAG laser system is a Class III device and must be approved for safety and effectiveness. Safety is relative and is dependent on the risk and benefits involved. Effectiveness requirements are not as rigid and do not require that the

device has to be the most effective, only that it is reasonably effective and not a sham.

As a Class III device, the laser must go through the IDE-PMA process to be approved. A research permit called an Investigational Device Exemption is necessary. This allows clinical data to be collected and trials to be conducted on humans. The IDE's are usually obtained by the device manufacturer, although an individual physician can apply to the FDA if he so desires. After the data is collected a premarket approval application (PMA) is submitted to the FDA. The PMA has to show that the device is safe and effective. In addition to the statistical clinical data, the manufacturer must show that they can build the device repeatedly to the same standard so that all their devices will be safe and effective. Manufacturers are required to comply to rigid manufacturing standards and the FDA is obligated to inspect the manufacturing facility prior to PMA approval. They also inspect on a routine basis to insure that proper testing is done and records kept.

After 1976 Congress passed the following subsequent legislation pertaining to the Medical Device Amendment of 1976:

Obligations of Clinical Investigators
21 CFR Part 54 (Proposed)
Obligations of Sponsors and Monitors of Clinical Investigations
21 CFR Part 52 (Proposed)
Protection of Human Subjects
21 CFR Part 50
Institutional Review Boards
21 CFR Part 56
Investigational Device Exemptions
21 CFR Part 812

The three main ones that the physician investigator should be concerned about are: the Protection of Human Subjects, which gives specific guidelines for the informed consent; the Institutional Review Board (IRB), which outlines its composition and responsibilities, and the Obligations of the Clinical Investigators.

The specific obligations of the clinical investigator are:

Obtain IRB approval of the protocol
Follow the protocol

Obtain informed consent from the patients
Maintain Records of patients
Maintain records on laser
Limit laser use
Provide records
Permit inspection

The clinical investigator can either develop his own protocol or use one prepared by the sponsor, to obtain IRB approval.

The FDA places much of the clinical responsibility on the Institutional Review Board which is also under FDA regulatory control. The FDA is very rigid about the informed consent form and have issued a guideline which outlines eleven items which must be included in the form. Proper and complete records must be maintained on the patients and laser. Laser use is limited to those investigators approved in the protocol and listed on the Investigator's Agreement. Progress reports are required by the sponsor for proper reporting to the FDA. The FDA may at any time inspect the hospital facilities and/or records of the physician investigator.

The elements of the IDE applications are:

Report of Prior Investigation
Investigational Plan
Manufacturing Practices
Non-commercialization Statement
Labeling

The Investigational Plan, among other things includes the physician's protocol. This should include who is going to be treated, patient criteria (exclusion-inclusion), the procedure for treatment, what results are expected and the method of measurement for success. It must also include a properly written informed consent form. The Investigational plan also states that an Institutional Review Board has approved the protocol and informed consent form.

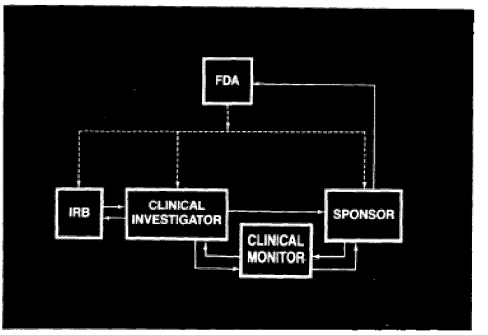

Fig. 1. Interaction between the group or persons involved in an IDE

Information should go from the clinical investigator to the IRB. The sponsor may also interact directly with the IRB. An example of the interaction is in the approval of a protocol. The clinical investigator writes the protocol and obtains approval from his IRB. They, in turn, return it to him. He then sends it to the sponsor, who submits it to the FDA for approval and informs the clinical monitor. Clinical monitor interfaces between the sponsor and the clinical investigators. Monitors may be comprised of medical and/or other personnel. They assure compliance and monitor all data for accuracy and completeness. The FDA may interact directly with the sponsor, the IRB or the clinical investigator.

19. UNDECIDED ISSUES ABOUT THE USE OF LASERS IN GASTROINTESTINAL DISEASE – PANEL DISCUSSION

Moderator: David Fleischer, M.D. Panel members: John Bowers, M.D., Steven Bown, M.D., Peter Bright-Asare, M.D., Larimore Cummins, M.D., Richard Dwyer, M.D., Dennis Jensen, M.D., James Johnston, M.D., Arthur Klass, M.D., Gustavo Machicado, M.D., Bergein Overholt, M.D., Paul Rutgeerts, M.D.

The use of lasers in gastrointestinal diseases is becoming more commonplace, yet there are several major issues about which there is not unanimous agreement. I thought it would be valuable to review with the discussants some of the major undecided issues regarding the use of lasers today. Through the course of the following discussion we will address the issues listed below: 1) which endoscope should be used and for what reason, 2) where should the endoscopic laser procedure be performed, 3) what type of anesthesia should be used, 4) which bleeding lesion should be treated, which bleeding lesion should not be treated, 5) in the case of the recently bleeding ulcer that has ceased bleeding under what circumstances is laser therapy indicated, 6) how do you train endoscopists to perform laser therapy, 7) should there be any limitations upon who should be allowed to purchase lasers, 8) are controlled trials necessary for the treatment of acute gastrointestinal bleeding, 9) is further animal work with lasers necessary and if so in what areas, 10) which gastrointestinal malignancies are amenable to laser treatment and which of these should be treated.

DR. FLEISCHER: Table I lists the endoscopes which are preferred by the different discussants. As can be seen the majority of discussants use a commercially available endoscope with two biopsy channels. The outside diameter is 13 mm. and each of the suction channels are 2.8 mm. However some investigators think it is important to have a larger channel. Commercially available endoscopes with 3.5 mm. channels can be used. In this situation the laser fiber goes down the single large channel and suction can be carried out around the fiber since most of the fibers are in the range of 2 mm. outside diameter. There is also prototype endoscope which is approximately 16 mm. in diameter and has both the 3.5 and 2.8 mm. channel. Some investigators think that this is ideal since the laser fiber can go down the smaller channel and the larger channel can be used for suction. The newer generation of commerically available endoscopes have an additional wash channel less than 1 mm. in diameter which can be used in addition to the regular biopsy channels. This can be attached to either water or gas and provides an additional cleansing capability.

TABLE I

ENDOSCOPES USED FOR LASER THERAPY
OF UPPER GASTROINTESTINAL BLEEDING

		MAIN ENDOSCOPE	ANCILLARY ENDOSCOPE
Standard two-channel	(2.8,2.8)/13 mm O.D.	7	2
Specialized two-channel	(3.5,2.8)/16 mm O.D.	1	2
Therapeutic one-channel	(3.5)/13 mm O.D.	2	3
Standard one-channel	(2.8)/7,8,11 mm O.D.	0	1
Other instruments		0	4

DR. FLEISCHER: Dr. Bowers could you comment on which scope you use?

DR. BOWERS: I use the Olympus GIF 2-T. I think having two suction channels is very important. Rarely we will use the Olympus TGF-2D which has a 2.8 and and 3.5 mm. channel but because the outside diameter is 16 mm. it is harder to use specifically with regard to the difficulty that some patients have swallowing that endoscope. For work in the colon we have used both the single channel and double channel colonoscope

DR. JENSEN: In addition to the routine endoscopes that others have mentioned on occasion, we have used less standard laser endoscopes. For example, for some lesions that are right at the gastroesophageal junction the old Olympus K scope which has an oblique angle seems to be beneficial in this regard. For lesions in the bulb and duodenum on occasion the duodenoscopes are the only ones that allow you to view the bleeding lesion. Finally on occasion we have taken some of the smaller pediatric endoscopes which have only one channel. In addition we have needed to attach a separate catheter to the outside to allow for decompression and gas removal. The tubes are usually taped proximal to the bending section. This allows the tip of the endoscope to get to the hard to reach places.

DR. FLEISCHER: Some investigators have used bronchoscopes for gastrointestinal procedures. Most of the commerically available fibers are 2.4 or 2.2 mm. outside diameter. Development is proceeding to produce even smaller fibers.

DR. KLASS: I use whatever endoscope is available at the time of the procedure. Sometimes it is more advantageous to use the smaller scopes

even if we have to tape a nasogastric tube to the outside for external suction.

DR. FLEISCHER: Although the commerically available laser units are theoretically portable and are buil on wheels, in fact since they are fairly bulky require special water supplies, and special electrical hook-ups most physicians keep the laser in one place. I would like to find out from the discussants whether or not they perform the laser treatments in their routine endoscopic suite,in the operating room or whether or not they have a modified and special endoscopic suite. Also do you agree that the lasers are not really portable or do any of you actually move the lasers from one spot to another?

The results of the discussants' positions are listed in Table II. It appears that most people perform the procedure in specialized endoscopic suites. However, it comes as a surprise to me that three of the investigators actually move the lasers from one side to another. Perhaps I can get some of them to comment on their views with regard to this matter.

TABLE II

LOCATION OF ENDOSCOPIC LASER PROCEDURE

Routine endoscopic suite only	1
Specialized endoscopic suite only	6
Operating room only	0
Endo suite & O.R. (transports laser)	3

DR. CUMMINS: The laser is actually based in our endoscopic suite. However, we have an electrical and plumbing set-up in the intensive care unitand the operating room so if the patient is particularly unstable the laser can be carried to the patient site. All the elective cases are done in the endoscopic suite. Dr. Fleischer,would you like to comment from the position of someone who has experienced having the laser in both a specialized endoscopic suite and in the operating room?

DR. FLEISCHER: When I was at the Veterans Administration Hospital in Washington the laser was kept in a special endoscopic suite. It was deemed special

as opposed to a routine endoscopic suite for it was larger than our routine endoscopic suite. There was monitoring equipment and if necessary an anesthesiologist could be brought to that room. In fact it was large and equipped like an operating room but was under the domain of the Department of Medicine. Since I have moved to the Cleveland Clinic I have been in a situation where the laser was already set into the operating room. This has the advantages that anesthesiologists are always close by and ready if necessary and there is a whole support staff that is on call 24 hours 7 days a week if needed. The disadvantage is that there may be scheduling conflicts with other departments who wish to use that particular room and secondly elective cases must be done there as well. This generally increase the cost and the time required for the more simple less extensive procedures.

I would now like to turn to the discussion of the use of anesthesia. I assume that everyone uses routine endoscopic preparation for the treatment of angiodysplastic lesions.

DR. JENSEN: In addition to Demerol and Valium we also find it useful to use glucagon for gut paralysis in certain patients.

DR. FLEISCHER: Does anyone use general anesthesia under any circumstances From sampling the panel it looks like the majority of you do not use general anesthesia for the routine upper gastrointesintal bleeding patient However, I see that some of you will have an anesthesiologist stand-by during the procedure if the patient is acutely ill and in some instances all of you have used general anesthesia for the patient who is extremely critical. There are some European investigators who routinely perform intubation for the patient with variceal bleeding because the bleeding is frequently so massive and the risk of aspiration is very great in that instance.

DR. FLEISCHER: There is general agreement among laser endoscopists that all actively bleeding ulcers should be considered for laser therapy. There is more controversy regarding some other lesions such as varices and hemorrhagic gastritis. I would like to ask the panel to discuss their positions as to which actively bleeding lesion should be treated.

DR. BOWN: We would treat a Mallory-Weiss lesion if it was bleeding but in our experience the vast majority of Mallory-Weiss lesions do not continue to bleed. We looked at our last 63 patients with bleeding Mallory-Weiss lesions and only one came to surgery because of persistent bleeding.

DR. FLEISCHER: Let's turn to the more controversial subject of acutely bleeding varices. Could I see the panel's feeling with regard to treating actively bleeding varices?

DR. RUTGEERTS: I think most Europeans including ourselves began treating the variceal bleeding with lasers. Initially the reported success was in the range of 90%, however the recurrent bleeding rate is so high that I do not think it can be considered as final treatment. Dr. Kiefhaber has treated more than 100 variceal bleeding patients with the YAG laser and reports a success rate of greater than 90% success. I believe that he follows the initial laser treatment with sclerotherapy because the rebleeding rate is so high. Other European physicians like Dr. Sander also has a high success rate with bleeding variceal lesions. We have now switched to initial management with vasopressin or Sangstaken tube and then proceed the sclerotherapy after they stop. Dr. Fleischer, didn't you publish a study on the use of lasers in varices?

DR. FLEISCHER: Our initial experience from a randomized controlled study was published in Gastroenterology as an abstract in 1982. Ten patients were randomized to laser therapy and 10 patients to sham treatment. We could stop the bleeding in 7 of 10 patients treated by laser and none of the variceal bleeders in the controlled group stopped spontaneously. However, the rebleeding rate was so high that when the final outcomes were assessed there was no difference in the overall outcome between the two groups.

DR. JENSEN: With gastric varices I think there is good rationale to use the YAG laser even if they continue to bleed. You may be able to stop the bleeding and then you can try and do something to decompress them. Sclerosis of gastric varices is difficult. Secondly, some of our animal data with the varices model suggest that it is fairly clear

that you can stop active variceal bleeding with the YAG laser, but it does not often result in obliteration of that varix. If you look at it a week later it is very often recanalized and there is not total obliteration of it. Sclerotherapy is the only thing in our model that has worked well. Based on that information if you had a YAG laser and you use it as initial treatment you could then proceed the sclerosis either at the same setting or at the next treatment time.

DR. DWYER: I have used the laser in certain patients to stop all the bleeding lesions that you have mentioned. I have used the Z-technique to treat variceal bleeding. By this method one zigzags around the peri-variceal area following the column of the varix. For diffuse hemorrhagic gastritis the YAG laser also may have a place. One uses lower energies and an enlarged spot size to treat more areas at once. Management of the diffusely bleeding neoplasm is very problematic by whatever treatment method is used. In some patients by treating the whole surface of the tumor you can stop the bleeding and also shrink the tumor which may have an additional role in decreasing the bleeding. So I will use the laser in any upper GI bleeding lesion that I find.

DR. KLASS: We have used the Argon laser for some patients with bleeding gastroduodenitis in patients with chronic problems. In several patients we have dramatically reduced the transfusion requirements.

DR. JOHNSON: There have been several instances where the patient has been labeled diffuse gastritis but the majority of the bleeding was primarily from 1 or 2 sites. In this case I think laser therapy would be appropriate.

DR. FLEISCHER: A review of Table III below shows that all of the discussants treat actively bleeding ulcers, angiodysplasia, Mallory-Weiss tears, and local sites on bleeding neoplasms. The majority do not treat actively bleeding varices although there is a split. More of the discussants do treat hemorrhagic gastritis than do not. There is an even split as to the appropriateness of the use of laser for diffusely bleeding neoplasms.

TABLE III

USE OF LASERS FOR VARIOUS ACTIVELY BLEEDING LESIONS

	YES	NO
Ulcer/erosions	10	0
Varices	3	7
Angiodysplasia	10	0
Neoplasm - diffuse	5	5
Neoplasm - local site	10	0
Mallory Weiss	10	0
Hemorrhagic gastritis	6	4

TABLE IV

USE OF LASERS FOR ULCER BLEEDING THAT HAS CEASED

	YES	NO	OTHER
No stigmata recent hemorrhage	1	9	-
Visible vessel	9	1	-
Adherent clot	5	1	4

DR. FLEISCHER: In terms of colonic lesions is there anyone who believes that acutely bleeding colonic lesions should be treated.

DR. BOWERS: We have treated some angiodysplastic lesions and some colon cancers in our patients.

DR. FLEISCHER: Dr. Machicado will you speak for the Los Angeles group and tell us how you prepare the patient with active colonic bleeding for endoscopic therapy?

DR. MACHICADO: We did a study to see whether emergency colonoscopy was feasible in patients that had massive hematochezia. Using an oral lavage saline preparation we have found that most patients can be done successfully after 2 to 3 hours of preparation. We were able to determine the bleeding site in over 80% of the cases. The lesions that were found were primarily dysplastic lesions of the right colon.

DR. FLEISCHER: Is there any risk of explosions in the colon using the lasers?

DR. MACHICADO: None

DR. FLEISCHER: Let's turn to the also controversial issue of the recently bleeding ulcer that has ceased bleeding. If a patient comes in with a bleed, and you endoscope him and find that he has a gastric ulcer that is not actively bleeding should it be treated? Let's take the instance in which you see a visible vessel, the instance in which you see an adherent clot, and the instance in which you see no stigmata of recent hemorrhage. Can I get your comments?

DR. BOWERS: Generally we treat visible vessels but there is one area in which extreme caution should be undertaken. The posterior wall of the duodenal bulb generally sits directly over the gastroduodenal artery. There have been several reports of laser induced injury whereby a non-bleeding or oozing ulcer was converted to massive arterial hemorrhage. Dr. Overholt has already addressed this issue and one that cannot be emphasized too frequently.

DR. JOHNSTON: I think you have got to temper each treatment for the clinical situation. I have stopped treating ulcers that lie over the gastroduodenal arteries or if there is pancreatic penetration.

DR. CUMMINS: Generally I treat the visible vessel but you cannot answer the question categorically. What I would suggest is the following approach. I divide up patients into those which I think will require surgery if the laser is not effective and those that may not require surgery even if the laser is not effective. I treat the visible vessel in the patient who will likely go to surgery because he has rebled or had multiple bleeds. On the other hand if I see a visible vessel and a bleeding ulcer for the first time I generally do not treat that patient since there is a possibility that you can incite bleeding and you can be responsible for the patient going to surgery.

DR. FLEISCHER: Dr. Bown you have written extensively on the matter of the visible vessel. Would you care to comment?

DR. BOWN: As we have written in a recent article in the New England Journal of Medicine we find that the likelihood of rebleeding from visible vessels is so great that it is appropriate that they be treated. Indeed there is now data in my group with both the ND:YAG and Argon laser that would suggest that there is a better outcome of patients with non-bleeding visible vessels that are treated.

DR. FLEISCHER: It can be seen from Table IV that the large majority of the panel considers it appropriate to treat a non-bleeding ulcer that has a visible vessel with lasers. There is also a strong feeling that ulcers that have no stigmata of recent hemorrhage should not be treated because the incidence of rebleeding is so low. The issue of treatment of the non-bleeding ucler that has an adherent clot is more complicated.

It is the fairly standard approach by endoscopists that do not do therapeutic treatment by any mode that the clot adherent an ulcer should not be washed away. On the other hand for those investigators who have therapeutic modality at their fingertips many would suggest that it is beneficial to get rid of the clot so that you can determine what is at the ulcer base. In that situation for example Dr. Bown would likely treat the area if he found a visible vessel after he washed off the clot. By contrast if no stigmata of recent hemorrhage were found underneath the clot (such as a vessel or a central spot) it would be unlikely for him to treat the lesion.

Let's now turn to the question which I think is one of the most difficult to resolve. How do you train endoscopists to perform laser therapy? I should mention that there have been courses held in the United States over the last three years where the attendees had the opportunity to both hear didactic lectures and work in the dog lab with lasers. Most have been very well received. It is very useful to have the opportunity to use the laser in animals in addition to hearing talks and seeing slides about it. Let me turn to the discussants.

DR. BOWN: In England we have not had courses like those which you describe in the United States, but I think they are an excellent idea. For the most part we have worked on a one-to-one basis where someone is attached to a unit. We demonstrate the procedure and the physician watches as we do it. It is simply the apprentice approach.

DR. RUTGEERTS: We have no formal training program but use an approach similar to Dr. Bown's. I think to affectively begin to use laser you will at least have to spend one month with a unit so that you can see enough active bleeding lesions to become comfortable treating them yourself.

DR. BOWERS: We really are not in the business of training physicians to use the laser. It is still an investigational device and I am anxious that the clinical results that we obtain are the best that can possibly be obtained. I would be uncomfortable sharing the treatment of my patients with someone else although I am happy for them to

observe me. I should point out that we do not regard the two-year program in gastroenterology which is the standard in the United States as adequate time to train physicians in laser endoscopy. It may be that a third year training in special endoscopic procedures would be the best approach.

DR. FLEISCHER: How did you learn to use the laser Dr. Bowers?

DR. BOWERS: By hook or by crook - that is by doing it myself.

DR. FLEISCHER: Did you start treating animals or humans?

DR. BOWERS: I was an experienced endoscopist before I began and I had experience with other forms of endoscopic surgery and some electrocautery, so I do not think the transition to using lasers was a difficult one. In terms of introduction to the laser I should point out that we have an established laser surgical unit and I took advantage of the people who were there and discussed the matter with them as much as possible.

DR. FLEISCHER: Dr. Jensen, you are a meticulous researcher. Do you think everyone should do dog work before they perform laser therapy on humans?

DR. JENSEN: If you are in Los Angeles you may have a difficult time getting hold of dogs with some of the new rulings in the city. But if you can get animals for experimentation I think it is a good idea. It is one of the four steps that we use to train our fellows. Let me address the broad issue then of how we train someone to use the laser. First comes the didactic part. This information can be achieved from either reviewing the literature that has been written on lasers or attending the courses you have alluded to in the past. Secondly, the dog lab. Most of our trainees have felt comfortable after they have treated about 50 standard ulcers and heparinized dogs and doing them endoscopically. After that they become facile with things such as depth perception and necessary treatment required for hemostasis. The third step is to involve them on treating some of the simpler bleeding lesions. These are patients that have small angiomata or those that have ulcers that are very slowly oozing. The fourth step is to do an emergency procedure. We try in our ow

fellowship just to train one person a year who is involved in this for the whole year but we are not in the business of training people from the outside either. I think it is incredibly difficult and important problem.

DR. FLEISCHER: Dr. Cummins you did not use the laser during your GI fellowship but now you have become one of the leaders in laser therapy in the United States. How did you learn to use the laser? I think you are in a situation that many gastroenterologists find themselves in today.

DR. CUMMINS: Well you know the story David and I am surprised that you asked. As you know I was flying my plane to a meeting in San Diego and the engine stopped. I glided down to an airport in Torrance, California and while the mechanic was fixing my plane I wandered over to Harbor General Hospital which is my alma mater. I went by the endosocpic suite at 11:00 on a Sunday night and found Richard Dwyer leaning over a patient. I spent the rest of the night watching him treat patients, He treated a 19 year old boy who was on his way to the operating room but instead of going to the operating room he comes out of the endoscopic room and goes back to his hospital bed. I was so impressed that I began to spend more time with Rich and develop some experience using the lasers in dogs.

DR. FLEISCHER: Dr. Bright-Asare, you did the majority of the work on one of the laser courses that we referred to in the past. So you have now been in the situation of attending one of these laser courses and setting one up. How do you train someone to perform laser therapy in humans, Peter?

DR. BRIGHT-ASARE: The physician has to be familiar with the principles of lasers, the endosconic procedure, and the technological equipment. The purpose of courses which are given such as the one sponsored by the Cook County Hospital in Chicago in 1982 was to achieve several goals. Firstly the didactic lectures were to give the fundamental of lasers and background information which is necessary. Secondly, I think dog work is absolutely essential. It gives you controlled environment where you can become familarized with the equipment. Because when you have a bleeding patient who is very critically ill

you don't have time to fiddle around with equipment. Next I think it is valuable to work with an experienced laser endoscopist for a period of about two to three weeks where you can learn and get on-site experience and hands-on experience with an expert. I don't think it is enough to merely write a protocol, convince your hospital to buy a laser, go to your institutional review board and begin treating patients. I don't think it is right. You cannot become an expert by attending one of these courses. For fellows and trainees in gastroenterology programs I do not think that a two year training program teaches you how to use the laser. It teaches you how to do endoscopy. I favor teaching of laser endoscopy as part of a third year program where special emphasis in put on therapeutic endoscopy. The ASGE should understand that therapeutic endoscopy is seldom learned in a three year program.

DR. FLEISCHER: Let me summarize my own feelings. The first thing to understand is that you really have to be committed to making a laser program successful in your hospital. It is different than when you begin to undertake a procedure that is new for you but already established (such as: colonoscopy or colonoscopic polypectomy). You have to understand that you are setting standards for your community. You have to understand the long-term implications, particularly with regard to other physicians that practice in your community. If the only training which establishes you as the laser expert in your community is the fact that you have gone to a three day course, then you are going to have to understand that if another physician in your community goes to a similar three day course then he should have the same right as you did to begin use of the lasers. I believe these courses are valuable but should be considered introductory. They are valuable in that they can give you a little bit of didactic background and some first experience with dogs. It is possible then for you to go back to your own community and either in a university setting or outside of a university setting to begin to work with dogs. This may require contacting a veterinarian in your community or surgeon with dog lab experience who can work with you in your own hospital. The next thing is self-training regarding diagnostic endoscopy that you do on patients that have acute gastrointestinal bleeding. In many patients we can see that there is blood in the

stomach but do not see the exact bleeding site. In preparation for the fact that when you use lasers you need to see the bleeding sites specifically, it may be useful when doing a diagnostic endoscopy to go through the maneuvers that are required to isolate the bleeding site. Dr. Johnston and Dr. Dwyer have referred to their methods in an earlier chapter. Next and ideally it would be best to spend some time with the so called laser expert. On occasion this could be arranged although currently in the United States there might not be enough "laser experts" to go around. Realizing that when you start out initially you won't feel entirely comfortable in your own setting you must proceed. My advice is to begin with the easier cases like small angiodysplasias rather than severe massive hemorrhage.

DR. FLEISCHER: Do the discussants feel that there should be any restriction on who can purchase lasers?

DR. JOHNSTON: At least in the United States anyone who is willing to follow the FDA guidelines which Dr. Enderby has outlined is legally entitled to purchase the laser. I would only like to underline what has been said previously and that is it requires a large amount of committment on the part of the physician and the hospital involved.

DR. FLEISCHER: Can each of you comment on what type of animal research you think would be most helpful?

DR. BOWERS: We need to develop animal models with pathologic states that are more similar to human conditions. For example, we have found that the standard ulcer-maker model may not closely approximate a bleeding arterial lesion in humans. When different animal models are developed then we can test the clinical situations more effectively.

DR. BOWN: I really don't think we can learn a great deal more from animal models for treating ulcer bleeding in humans. Some of the work that Dr. Jensen and others are doing with regard to variceal models in animals may prove very valuable in humans. For tumor therapy, a vast amount of work needs to be done.

DR. CUMMINS: We need to look a lot more at tissue variables which determine laser effect.

DR. DWYER: The area of dosimetry needs to be explored more.

DR. JENSEN: More work needs to be done with the evaluation of hemostasis of bleeding lesions in the colon. There is also more work to be done with the hemostasis of varices. More technologic advancements are necessary in regards to testing of laser scalpels and various fibers.

DR. KLASS: The use of hematoporphyrins in gastrointestinal malignancies has not been studied.

DR. OVERHOLT: We need to learn more about the control of bleeding from large arteries. Most of the work that has been done today has been with small oozing capillary lesions.

DR. FLEISCHER: As the penultimate point of discussion I would like to turn to the endoscopic laser therapy of gastrointestinal malignancies.

DR. BOWERS: I think that there are two areas in which laser therapy of gastrointestinal malignancies in humans is appropriate. Firstly, I think it should be regarded essentially as a palliative therapy. The only possible exception is in those patients who are not surgical candidates and who have local problems which require treatment.

DR. FLEISCHER: I think that sums up my own feelings. John what about benign polyps?

DR. BOWERS: As you know I treat benign polyps with lasers and I restrict my therapy to those circumstances where the polyp is not easily removed by standard techniques such as snare electrocautery. Additionally I will treat those patients who either elect not to have surgery or in whom surgery is not possible.

DR. FLEISCHER: Dr. Bown which GI malignancy should be treated. Should we treat a carcinoma of the stomach in someone who is a moderately poor operative candidate but who is not obstructed.

DR. BOWN: No, we only treat people for palliation. I think it should be used for advanced tumors causing obstruction or bleeding and those who are unsuitable for surgery. As a separate indication I would consider using it for small sessile polyps not suitably removed by snare treatment.

DR. FLEISCHER: Unfortunately we have not included a Japanese

investigator as one of the discussants on this panel. There is a lot of work going on treating gastric tumors for both palliation and cure in Japan. Some of the studies are outlined in Chapter XI.

DR. FLEISCHER: Finally I would like to ask the discussants whether or not they think controlled trials are still necessary for the use of lasers with regard to treating acute gastrointestinal bleeding.

DR. DWYER: It seems clear to me that lasers are affective in achieving hemostasis. You can look through an endoscope, fire the laser and see that you can stop active GI hemorrhage. I have yet to see the controlled studies evaluating the use of hemostats for controlling bleeding. Hemostats work and so do lasers. Further studies in this area are not necessary. We can better spend our time looking at new areas in which lasers can be used in the treatment of gastrointestinal and non-gastrointestinal diseases.

DR. BOWN: I feel very strongly that controlled trials are necessary. There is not enough firm data on the natural history of this condition and we must carry out controlled trials. There is so much discussion on the relative merits of what is being reported from all different units and I believe that only controlled trials can give us the answer that the whole medical community will believe.

DR. JOHNSTON: Until a few months ago I wasn't certain whether or not more controlled studies were necessary for gastrointestinal bleeding. However it was only when I started reviewing the literature on the natural history of gastrointestinal bleeding that I found the only good literature comes from the information with the controlled trials. The rest is far less valuable. It is similar in many ways to the cimetidine studies that were done for treatment of ulcers. From those studies we learned a great deal of factual information that was not available before those trials were done.

DR. CUMMINS: You must realize how each of the controlled trials is designed. If you have a controlled trial that fails to demonstrate the efficacy of laser therapy you have to realize that the study is usually designed to measure one of two things. One is the efficacy of the machine and the other is the technique of the endoscopist.

DR. FLEISCHER: I am certainly very greatful to the discussants. We have covered a lot of subjects which are not generally discussed in standard textbooks or at didactic courses. I have tried to get the panel of experts to confront some of the gray issues in laser endoscopy. As the field evolves, firmer data will be available and opinions will be less necessary.

20. CURRENT LIMITATIONS, NEW TECHNOLOGICAL DIRECTIONS AND AREAS OF INVESTIGATION – PANEL DISCUSSION

Moderator: Dennis Jensen, M.D. Panelmembers: Stephen Bown, M.D., John Bowers, M.C., Denis Cortese, M.D., Larimore Cummins, M.D., Charles Enderby, Ph.D., David Fleischer, M.D., James Johnston, M.D., Arthur Klass, M.C., Gustavo Machicado, M.D., Paul Rutgeerts, M.D., Fernando Villa, M.D.

DR. JENSEN: Practitioners of laser medicine, particularly gastroenterologists, need to define which patients will benefit from treatment through the short and long term duration and what are the limitations and guidelines for the application of lasers and other costly devices in these patients. For each UGI bleeding lesion, we need more information about natural history, pathology and the best therapeutic instruments to use. Although there is considerable new information from controlled trials about bleeding peptic ulcers, visible vessels and other stigmata, similar detailed natural history and pathologic information should be defined for varices, angiomata, Mallory-Weiss tears, mucosal lesions and tumors. Such information would allow us to better focus valuable resources and medical talent to help high risk patients. For lower GI bleeding, the natural history has to be worked out. We need to have more information on what should be the role of invasive endoscopy, therapeutic endoscopy with whatever modality. For tumor treatment compared with standard techniques (radiographic, angiography, surgery) for diagnosis and treatment in GI, whether upper GI or in the colon, guidelines and limitations must be defined rather than remaining empirical.

For industry, several tasks require further work. We need improved delivery systems, including not only fiber technology for YAG and Argon lasers, but also for CO_2 lasers. Can medical lasers for gastroenterology be made smaller, portable and cheaper? The current technology is not such that you could put a YAG or Argon laser in a suitcase and bring it to your patient or to a hospital and take it in the afternon to some other hospital. Endoscopes could be improved for laser use for example in GI or pulmonary.

None of them are ideal. New developments have to take place to facilitate therapeutic endoscopy with lasers and other devices. The endoscope companies are lagging behind in the development of therapeutic accessories and more research and development by them will be required. Improvement in training and research in laser medicine should be encouraged. Sponsorship of conferences and clinical studies by industry and academics may facilitate this end. Undoubtedly over this decade, there will be an evolution in patient care, training, and research in laser medicine.

What about tastks for the federal government? The U.S. government has put a fair amount of money into regulation but not much money into clinical studies in laser medicine. Lasers are being applied empirically in patients. We need much more information about laser's impact on outcome, the cost accounting, and the best way to allocate them before they become the standard of care. The federal government perspective must change so funding is available for studies to answer these questions. Industry has become more interested in these questions while the government has sought legal control.

DR. JENSEN: Fiber technology. What noeeds to be done? What are the current limitations? For YAG of argon, what does Dr. Stephen Bown think is necessary to obviate some of the problems that he's had in his studies and to improve fibers for everybody?

DR. BOWN: I think the real problem is the damage to the fiber. Its been our eternal frustration for the last three years. We need more rugged fiber delivery systems and systems which are cheaper and can be repaired at home if the tip is damaged, by the physicians or technicians. As important, we require versatile fibers that can be used in different laser endoscopic applications such as in the GI tract, the lungs, and bladder. In general we need cheaper fibers that are easier to repair and more versatile.

DR. JENSEN: Dr. Art Klass, what is your opinion about HAG laser and also about the CO_2 delivery system?

DR. KLASS: Like everyone else, we have had fibers breaking. We no longer use prepackaged fibers, but instead our laser technician can

recleave a fiber for Argon or YAG laser application in a matter of minutes. Personnel and lasers are in a special laser center in the hospital. We've had some problems with endoscope damage in cancer work while using much higher power and much longer pulse durations than GI hemostasis application. The reasons are unclear. Perhaps there is some cleavage within the fiber and side leakage accounts for the damage to the endoscope during teatment. Further study is required and we plan to initiate detailed studies. In terms of the CO_2 fiber delivery system, there is a lot of work going on around the world and a number of flexible CO_2 fibers are available. Many of them are too thick to be used transendoscopically. Our biophysicist, Dr. Terry Fuller, has designed a fiber which is now one meter long and will go through the biopsy channel of a therapeutic panendoscope. Clinical applications have been initiated with it. There may be some problem with this CO_2 fiber if any cleavage occurs and some noxious gases are leaked.
(These are used in the manufacture of the fiber.) Dr. Fuller has applied for FDA approval. Once he gets FDA approval, there will be commercially available flexible CO_2 fibers, at least for the shorter endoscopes. The sky is the limit, in my opinion, for CO_2 laser applications. Dr. Fuller has initiated studies with CO_2 laser for tumor treatment in areas of the body such as the oral cavity and vagina. It is his bias that the CO_2 laser will be the preferential mode for debulking large tumors.

DR. JENSEN: Dr. Charles Enderby, in the next ten years, how do you think the YAG laser fiber or delivery system will change so that the gastrenterologists, pulmonary specialists and others will be more pleased with it?

DR. ENDERBY: It's hard to say what will happen in 10 years, but we are making a lot of progress right now. We are modifying the current fibers so they have different metal tips which reduces the damage to the fiber itself. We have developed tips so that repair of damaged fibers is relatively easy in the laser unit. It is almost impossible to keep everything off the end of the fiber so some damage is inevitable. We see the trend toward smaller laser fibers since the endoscopes tend to get smaller all the time. We are de-

veloping smaller fibers that will work in smaller biopsy channels. As far as cheaper fibers, it's hard to say. We know that physicians don't want to spend that much money on fibers and we are going to try to reduce the cost of the fibers themselves.

DR. JENSEN: There has been a question about current limitations as far as accessibility of lesions such as bleeding UGI lesions. Paul Rutgeerts, what improvements could be made to make more lesions accessible to laser treatment in the upper GI tract?

DR. RUTGEERTS: That is a problem, but I think that smaller endoscopes may be more useful to find all lesions. Secondly, it would be possible and advantageous to have an endoscope whose viewing angle was adjustable, for example, from a forward viewing to a side viewing. The flexibility of endoscopes is a problem particularly with couble channel large caliber endoscopes. Improvements are needed so that thin endoscopes have large suction channels and yet remain very flexible. But there will still remain some difficult areas. Several endoscopes will be necessary and several different lasers fibers.

DR. JENSEN: Dr. Jim Johnston, what are your comments as far as accessibility of UGI lesions for treatment endoscopically?

DR. JOHNSTON: The biggest problem I have is with the large fixed clots of blood that obscure lesions. Somebody needs to develop an efficient means of either dissolving those clots or liquefying ther so they can be suctioned. Also, a method of differential suctioning needs development to efficiently suck large clots out without damaging underlying mucosa. Then the underlying bleeding lesions can be exposed and treated.

DR. JENSEN: Dr. Cortese, are there lesions that you have trouble getting to with bronchoscopes? What are your comments on accessibil ity and improving those in the tracheobronchial tree? Also, comment on the current technology pertinent to pulmonary endoscopic laser therapy.

DR. CORTESE: With the type of tumors we are dealing with, the accessibility is not much of a problem because the lesions are within

the reach of the flexible bronchosope. Endobronchial lesions within the upper lobes can be the hardest to reach but technology is excellent. The biggest problem is when they are close to the vocal cords and we have trouble maintaining an airway.
In regard to fiber technology, we have been very pleased with the new polishing technique for fibers that Molectron has taught us to use. We polish each fiber after each case and sometimes use up to four fibers per case. Since we limit tumor treatment to no more than about 7,000 joules per fiber, we have not damaged the YAG fibers. Our Argon laser is a large laboratory laser and requires engineering support. It could be improved so that physicians could more easily use the system. The typical surgeon or physician wnats to throw a switch and use the device rather than really becoming an expert in lasers. Improvements are indicated.

DR. JENSEN: The current status of lasers in medicine is that the directing physician must become an expert on all aspects of the laser. If one becomes a laser doctor, he will get involved in laser optics and other subspecialty areas whether he planned to or not. If one is not knowledgeable about fundamentals and technology of lasers he is going to have many problems. Lasers are high technology devices. They are expensive and require routine care. Someone must have more than a pedestrian interest to be a laser physician. Dr. Enderby, what is the likelihood that we will have GI lasers for coagulation that can be easily carried around?

DR. ENDERBY: Anything is possible, but I know what goes into this Molectron YAG laser that weighs over 800 pounds. It can be rolled onto an elevator and moved to deifferent locations within a hospital without getting out of alignment. I do have a hard time seeing it fit into a suitcase by the end of the next two years, but I would hate to say it can't be done.

DR. JENSEN: What is the size limitation? Is it technical, financial or something more fundamental?

DR. ENDERBY: There are some things that just take a certain amount of size. With enough money, some parts could be reduced in size, but other parts such as water pumps are large because of the cooling

requirements of the YAG laser head. With enough money, obviously those could be broken down to size.

DR. JENSEN: Do you think the Japanese are going to miniaturize GI lasers as they have miniaturized other things?

DR. ENDERBY: They haven't so far. The Japanese lasers that I have seen are bigger than the ones we have here.

DR. JENSEN: Dr. Enderby, regarding the FDA situation in the United States, what do you predict over the next decade will be the classification of YAG laser use? in gastroenterology, pulmonary, and urology?

DR. ENDERBY: We are hopeful that the YAG laser will be approved for general use very rapidly in some areas. As investigational devices in these subspecialties, each laser device has to be approved for each new medical application. Some medical applications are easier than others to prove safety and efficacy. We are proceeding one step at a time. I see it moving fairly rapidly. We have a lot of medical cases being reported to us now. When the statisticians feel that we have the significant results, I would anticipate that general approval would happen very rapidly. It certainly would not take ten years.

DR. JENSEN: Dr. Gus Machicado, in the lower GI tract, are there modifications that need to be made in the endoscopes to facilitate therapeutic colonoscopy?

DR. MACHICADO: We do need to some improvements in colonoscopes. More flexible colonoscopes, smaller in diameter, and with a larger suction channel would help. Localizing some of the angiodysplasia in the right side of the colon and positioning these for laser or coagulation probe treatment can be very difficult with currently available colonoscopes. It would be helpful to have an oblique or side viewing colonoscope which could reach some of the blind areas in the colon. I think that modifications for diagnosis and treatment during emergent colonoscopy certainly will be required.

DR. JENSEN: Jim Johnston, for a colon bleeding lesion, such as a 1 cm cecal telangiectasia, do you think it is going to be standard medical care to diagnose and treat such lesions via colonoscopy? What do you think the treatment of choice is going to be?

DR. JOHNSTON: The whole problem is accessibility in patients with severe hematochezia. I haven't had the luck you have had with purges and emergency colonoscopy but I haven't tried as hard. If we can cleanse the colon, there is no reason we can't treat there as well as we do now in the upper GI tract. If we can have an endoscope that will allow us to get into the small bowel, there is no reason why we can't treat that also.

DR. JENSEN: Dave Fleischer, can I have your comments on treatment of bleeding lesions via colonoscopy?

DR. FLEISCHER: The way therapeutic endoscopy is moving is toward a technology which allows endoscopists to treat lesions that previously required surgery. We have to have better washing systems, better ways to evacuate blood, and better ways to administer the endoscopic treatment.

DR. JENSEN: There are a number of questions about multi-purpose laser units.
Dr. Art Klass, your hospital has a large laser unit. As a gastroenterologist, what problems have you had getting access to lasers for emergency treatment? When you have a laser that has multipurpose use, how do you see the gastroenterologist being able to use it? If you can't use a laser for GI bleeding, what do you do?

DR. KLASS: If you are going to try to get your hospital to buy a YAG laser and to prepare the room for it, the minimum investment will be $150,000. If the laser is purchased out of public funds, you can't justify the use for bleeding alone for one to two cases per week. You have to be able to show your administrator that there are other areas in which the YAG laser is going to be use ful. Malignancy treatment with YAG is going to be an important area and there will probably be gynecological and urologic applications. For a multidisciplinary approach, several lasers and perhaps back-up equipment may be necessary to avoid delays. If a YAG laser malfunc-

tions in our laser unit, we have either an Argon or a second YAG as a back-up as well as a laser physicist and a skilled laser technician available. Right now there are about 2,000 scheduled laser cases a year in my hospital. When I have a bleeder, I either have to wait or bump somebody who was scheduled to do an elective procedure. GI bleeding is the only area of laser use currently which is not elective. Everything we have done up to this point until tumor work comes along is an emergency. Our laser labs and the O.R.'s are scheduled day by day. Cases are scheduled weeks in advance by gynecologists, plastic surgeons, dermatologists, ENT people, and so on. As a consequence, I have done a lot of electrocoagulation work for treatment of GI bleeding. I may not be able to wait twor or three hours for the O.R. or the laser unit to be cleared. A lot of the bleeders I do after hours, nights and weekends because that is the only time that you can have two or three hours. Others have emphasized the fact that you should not have to fight the clock. It is bad enough to deal with all the technical problems and the clinical problems with your patient. You should not have to be in a position to fight the clock where you have one hour or 1.5 hours scheduled and you've got a problem which will take three to four hours. All your colleagues will be breathing down your neck because they have out-patients, in-patients, and other time constraints too. You are going to run into these kinds of major problems when you develop a large laser unit. Tumor work, such as treatment of partially obstructing esophageal or gastric malignancies is time consuming also and requires a minimum of trhee initial treatments a week. With every other day treatment, three reservations for 1.5 hours and at least 0.5 to one hour to clean up the room wil be required for each patient. These are details about a laser unit which require O.R. type coordination.

DR. JENSEN: John Bowers, you have been working a unit that has multiple lasers. Do you think that if people from a larger community and a larger hospital have the choice that they should get more than one laser? Should they get a CO_2 laser, an Argon laser, a YAG laser and also a back-up of each?

DR. BOWERS: The whole idea of a laser unit for multiple use with different lasers is to try and make the whole operation cost-effective. It is an expensive proposition and, when you have multiple lasers, at least the personnel, equipment and space can be shared and that saves some money. Ultimately high utilization and sharing expenses is the major thrust that allows us to pursue a multidisciplinary approach. Also, I think different lesions require different kinds of lasers and it is possible to have all the modalities at your disposal in a multidisciplinary unit.

DR. JENSEN: Dr. Cummings, you are an expert on the YAG laser in gastroenterology and work in a moderate sized community hospital. Are you going to start working with CO_2, Argon, and Ruby lasers?

DR. CUMMINS: No.

DR. JENSEN: Why? Are they needed in a community hospital?

DR. CUMMINS: I personally am not going to be involved in argon because of the technical difficulty. There are utilizations for Argon laser. For some applications Argon laser may have advantages. There are several indications for both types of lasers in GI.

DR. JENSEN: Jim Johnston, you said your YAG laser for just GI was not cost effective. Would you make a recommendation to the people in a farily larege community hospital as to what practically if anything they should do to get other people involved with other YAG laser applications?

DR. JOHNSTON: Lasers have been so new that you really have to have someone with a research mind and interest to get them interested at this point. That will be less of a problem once these indications are more established. But I think you've got to have a multispecialty approach to justify a laser in a community hospital at this point.

DR. JENSEN: Queston and answer periode. Question: Who other than Molectron makes YAG lasers?

DR. ENDERBY: The following companies make YAG lasers: Molectron, Medilase, Bard Stroud, Pentax, and Olympus. Cooper Medical makes Argon laser. Fourteen different companies make CO_2 lasers.

DR. JENSEN: Question: How do the electrical and water outlet requirements differ for these lasers?

DR. ENDERBY: The electrical requirements for the Argon and YAG are very similar; they both take 208 volt three phase. The water requirements for argon are a little more severe than the YAG; it has to have a continuous flow of water. For CO_2 laser, it's a much lighter electrical requirement and the instruments can be plugged right into the wall socket. CO_2 lasers are air cooled and are more efficient and portable.

DR. JENSEN: Dr. Cortese, could you comment about the use of the Argon laser for treating interbronchial tumors?

DR. CORTESE: The argon wavelength is absorbed by blood. In our experience, argon has not been very good for treatment of endobronchial tumors. We use the Argon laser to pump a dye laser which is useful for detection of small endobronchial tumors.

DR. JENSEN: Dr. Enderby, what is a pumped dye laser?

DR. ENDERBY: For the tumor work, they want to get red light. The way you get red light is to take an Argon laser and you use that to excite the dye laser which is another type of laser. It is a liquid laser and uses a dye as the lasing mechanism. In pulmonary tumor work, an Argon laser is used for excitation of the dye laser which produces a very intense red light. That red light activates a chemical of dye which had been given to the patient and is taken up by the tumor. Onycolysis (treatment) is possible or fluorescence (for diagnosis) depending upon the chemicals injected and the wavelengths of lasers used.

DR. JENSEN: Dr. Fleischer, would you treat an esophageal carcinoma with complete obstruction as opposed to one where there is a minimal lumen?

DR. FLEISCHER: If there is any lumen at all, I always feel more comfortable. I've treated a couple of people that were completely obstructed with trepidation. You can use CAT scans to map out the esophagus. Generally, I start treatment with YAG laser in the middle or the most central area. After you do that, you can usually identify some lumen. What some people are doing is putting a biopsy forceps or plastic catheter inside the lumen and using it as a guide. After you start treating esophageal tumors with YAG laser, a lot of edema develops and the lumen may completely close. That makes it more difficult to get down below the area of occlusion. I usually just wait a day or two and that tissue can slough off or can be removed.

DR. JENSEN: For YAG laser treatment of esophageal cancers, what powers are you using?

DR. FLEISCHER: I'm using about 90-100 watts for 2.5 seconds. I don't have access to an Argon laser. But for the theoretical reasons that we've talked about, I don't think it would be nearly as good for treatment of obstructing tumors.

DR. BOWN: We have used the Argon laser te re-cannalize the gastric outlet obstructed by a carcinoma. It certainly does work, but you need to use a very high power level, such as 8 to 10 watts for effective vaporization. You don't get the same depth of necrosis that you do with the YAG laser, so the lumen you create may take significantly more time. But definitely you can use it.

DR. JENSEN: There's been a lot of discussion about techniques and setting for YAG lasers, nobody has talked about techniques and setting for Argon lasers. If you were to treat an ulcer in the stomach, what would your setting for Argon laser be?

DR. JOHNSTON: In referring to the article that you and I wrote from our dog work. (It is in Gastroenterology) Eight to 10 watts is what we uesd for spurting arteries with adequate CO_2 at the target set ahead of time so you can blow the blood away. We actually use a manometer to set the back pressure. Treatment distance for actively spurting lesions must be within 2 cm. To prevent vaporization, you have to be further away than 5 mm. We use a two channel therapeutic

panendoscope for severe UGI bleeders. Treatment of angiomata is less of a problem. You can treat from a greater distance with less power (5 to 7 watts). In the colon, for oozing lesions such as angiomata, we use 5-8 watts. You don't have to use much coaxial CO_2 if you are treating oozing or non-bleeding lesions.

DR. JENSEN: Is Argon laser useful for GI tumor treatment?

DR. KLASS: For smaller tumors or obstructions it can be used effectively but may take more time. I would just like to make a brief comment on the use of Argon laser for bulky tumors of the gut. W did some work with vital dyes that might enhance absorption of the specific laser wavelengths. For example, sodium fluorescene is readily available in sterile ampules and can be injected into a tumor mass. It will enhance the absorption of the argon wavelength and presumably one will get much better tumor necrosis. We are going to try this approach if we have the patient scheduled for endoscopic tumor resection and the YAG is down.

DR. JENSEN: When you are vaporizing tumors in the colon, is there concern about an explosion=

DR. BOWERS: If the heat exceeds the ignition temperature of gases in the colon, an explosion could result. To my knowledge that has never occurred with laser. We recommend adequate preparation before laser treatment. Our preference is to use a saline purge prep which is very effective in reducing the concentration of all those gases from bacterial metabolism. Once you've cleared all the stool out, most of the bacteria are gone.

DR. FLEISCHER: How about the use of glucagon for upper and lower GI bleeding)

DR. JENSEN: We use it for control of motility, very commonly in the duodenal bulb, antrum and also colon. I don't know what the effect actually is an visceral blood flow. Someone mentioned to me that glucagon increased visceral blood flow but I'm unaware of good studies on that. How much do we use? Just like ERCP, 0.5 mg and repeated as necessary.

DR. JENSEN: Are there any limitations of transporting bleeding patients to the laser for treatment?

DR. JOHNSTON: That is one thing that slipped through the discussions. When you set up a laser in a community hospital, you're not going to treat just the people in your hospital, but you're going to treat the whole community and transfer patients form one hospital ICU to another for treatment. That carries certain risks. I felt uncomfortable with that. The people who need it the most are the biggest bleeders and they have the greatest danger of exanguinating or having an arrest on the ambulance on the way over. I have not found a good way of resolving that yet, but it is a danger you ought to recognize.