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ARMED FORCES-NRC COMMITTEE ON VISION

LASER EYE EFFECTS (U)

Report of Working Group 25

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PREFACE AND RECOMMENDATIONS

At the time of the 1965 meeting of the Committee on Vision, I was asked to be chairman of a working group to study laser eye effects related to military and laboratory applications and to recommend safety measures, protective devices, and continuing research to support those areas. The results of the working group's efforts thus far are presented here under six topics: technical characteristics of lasers, laser-eye pathological effects, laser-eye functional effects, personnel protective measures, devices for eye protection and eye examination and treatment standards.

The chairman's recommendations derived from the group's discussions and culled from the following sections are as follows:

A. Research Recommendations

1. A program should be established to standardize on criteria of retinal damage from light exposure and on radiometric calibration procedures. Data from the laboratories of Geeraets and Ham, of Fine and Zweng, to name four workers in this area, disagree by substantial amounts. It seems that the trouble lies with the interpretation of pathological materials to determine when threshold damage has occurred. There is also a strong possibility that these laboratories differ in their energy calibrations.

2. It is highly possible that irreversible effects occur below the level of observable pathology, which may nevertheless be detectable by electron-microscopy or by enzyme stain techniques. It is recommended that programs be continued: (a) to identify and define the energy levels at which these microscopic changes may occur, (b) to relate these to amount of visual loss, and (c) to define criteria for standardizing these effects.

3. Controlled studies of long-term effects and the effects of repeated exposures on the cornea, iris, lens, ocular media, as well as the retina and choroid, should be undertaken. Data have been presented that indicate laser exposure has an impact on all of these structures.

4. The laser hazard slide rule should be verified for wavelengths other than ruby.

B. Safety Recommendations

1. A standard sign should be adopted to clearly delineate laser spaces.

2. All personnel who will be in the vicinity of lasers and laser spaces should be indoctrinated on the hazards of laser equipment.

3. Industrial devices should be equipped for indirect viewing wherever possible.

4. A fail-safe interlock system should be developed for surgical and machining devices to preclude the possibility of accidental exposure of the operator and others in the operating room or laboratory.

5. Manufacturing standards should be established to insure that under normal conditions the user has a safe instrument.

6. Those first coming into laser work should receive an eye examination such as described in Section VI to serve as a reference base for further periodic examinations and for examinations in the event of exposure.

C. Safe Exposure Levels

The most significant and also most difficult to deal with topic of this report is the question of what is the maximum permissible dosage of laser radiation of the different wavelength transitions that can safely be permitted to reach the eye. Those dealing with the application of lasers in the field or laboratory, in the government or institutional setting, are concerned with allowing operators to perform their assigned tasks with a minimum of interference, at the same time that hazards are minimized. Complaints have been voiced, particularly with regard to military field devices, that the provisional safety standards which have been set preclude the operation of the devices. It is hinted that in the face of this situation people are ignoring safety precautions in order to perform their tasks. It is therefore urged, from all quarters, that reasonable safety standards are needed as a basis for sound operating procedures. The heart of this question is: what is the maximum safe dose? As will be seen in Chapter II of this volume, there is considerable evidence which is in fairly good agreement on the threshold dose of the ruby laser pulse that produces a minimally observable lesion, as viewed with an ophthalmoscope. From those data, the value 0.8 joules/Cm^2 on the retina has been stated and widely accepted as the minimum dose producing observable damage by that technique. As seen in Chapter II, when giant-pulse laser radiation is used, the minimal ophthalmoscopic lesion is produced by .07 joules/Cm^2 on the retina. The latter value appears to hold between 5 and 50 nanosecond pulses. These threshold levels have been projected to the cornea by computing the energy at the cornea which would produce the threshold retinal irradiance in a minimum sized retinal spot. Assuming a night-adapted pupil, these values are 1×10^{-6} joules per square centimeter in the plane of the cornea for the non-q-switched pulse and 1×10^{-7} joules per square centimeter at the cornea for the giant pulse. As a provisional safety standard, the Army[1] has added an additional safety factor of 10 in promulgating these values as allowable safe corneal irradiance levels.

Beyond the results for ruby laser, as may be seen in Chapter II, results thus far on neodymium laser pulses show that 5 to 6 times more energy than from ruby is required to arrive at the minimal retinal lesion with this transition.

For continuous wave gas lasers (helium-neon), there is no evidence on which to base a threshold number for minimum retinal damage. The Lawrence Radiation Laboratory[2] Makes extensive use of continuous wave lasers in optical alignment applications, so they have formulated a safety standard based on allowing a maximum of 1 degree centigrade rise in temperature at the retina. They arrive at a figure of 1×10^{-6} Watts/Cm^2 at the cornea, which they state as a tentative maximum safe level for exposure to continuous wave helium-neon lasers.

The foregoing numerical results must be considered valid only for grossly observable thermal effects on the retina. As will be pointed out in Chapter III, the problems of flash blindness effects on the receptor mechanisms of the eye as produced by laser exposure are totally different. In addition, between the extremes of retinal burn on the one hand and levels which we know produce completely recoverable flash blindness on the other, lies an almost totally unexplored range which we estimate to be from 1 to 3 log units of irradiance over which more subtle damage to retinal tissue, particularly the receptor cells, may be encountered. Continued vigorous research to obtain information on effects over this unknown range has been recommended above and is strongly urged.

Finally, the Working Group has decided to call the reader's attention to the above cited threshold burn values which are the best available information on the maximum allowable irradiance at the cornea. It does so without recommending that these values be adopted as the basis for any long-term safety standards. It is our continuing, and much debated, view that too much evidence is missing to allow us to state maximum safe dose levels with confidence at this time.

The chairman is grateful to the members of the Working Group for their efforts.

H. G. Sperling

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CHAPTER I

A REVIEW OF TECHNICAL CHARACTERISTICS OF LASERS

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INTRODUCTION

Since Maiman first succeeded in obtaining laser action in a synthetic ruby rod in 1960[1], the discovery of new laser transitions has proceeded at a very rapid pace, so that today one would scarcely try to count the number of wavelengths at which laser action has been observed. A few of the more promising lasers have received intensive development effort, which has led to some rather remarkable achievements in terms of power, coherence, lifetime, and other characteristics. Concurrent with these improvements there has been a steady increase in the numbers and types of lasers in research, education, industry, and military applications. There is every indication that the use of lasers will continue to expand and that human contact with lasers in research, teaching, and other activities will increase enormously in the next decade.

To aid in the detailed discussions which follow in the later chapters on laser eye effects, a review is given of the characteristics of lasers and of the radiation emitted by them. Certain properties and principles of operation are common to all lasers, but others are best treated by considering the three main laser classifications, solid state, gaseous, and semiconductor.

A brief statement of the present capabilities of lasers is in order. Solid-state giant pulse (Q-switched) lasers, such as ruby and neodymium, produce pulses that are on the order of 5 to 50 nanoseconds (1 nanosecond equals 10^{-9} seconds) in length with peak powers of the order of 10 to 1000 megawatts and pulse energies, typically, from 0.1 to 10 joules. Alternatively, the same lasers operated in the normal or "long-pulse" mode generate pulses on the order of a millisecond in length, peak powers up to hundreds of kilowatts, and pulse energies from a few joules to a few kilojoules. Such "long-pulse" operation is typically about an order of magnitude more efficient than Q-switched operation, although neither is particularly efficient in converting electrical input energy into laser energy. Most work requiring high power has been done in the red (chromium-in-sapphire or ruby, 694mμ) or near infrared (neodymium-in-glass or crystals, 1060 mμ). The most common of the continuous (CW) lasers is the helium-neon gas system which has its principle lines at 633 mμ, 1150 mμ and 3390 mμ. The output is usually a few milliwatts but can be as high as a few tenths of a watt at 633 mμ. The argon-ion laser, which is presently capable of several watts CW in the green (principally 488 and 514.5 mμ),

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**Department of Surgery, Tulane University School of Medicine, New Orleans, Louisiana is now becoming increasingly common as technical problems are overcome. Still higher continuous powers are available at 1060 mu using nd^{3+} in yttrium-aluminum-garnet (YAG), and an output of over 200 watts has been reported. Perhaps the simplest of the CW lasers is also capable of the highest average power; the CO_2 molecular laser oscillates at 10.6 microns and can produce about 50 watts in a very elementary design, and kilowatts or more in larger or more complex systems. Furthermore, because of the relatively long lifetimes in the lasing levels of the CO_2 laser, it can be Q-switched to produce peak powers many orders of magnitude greater than the CW power from the same laser.

A summary of the present capabilities of the more common lasers obviously cannot include reference to most of the specialized systems in use in research or various special projects. However, it is important to note that higher peak powers can be obtained from some of the CW lasers by pulsing the pump power or by Q-switching the laser cavity, or both. Other lasers can only operate in the pulsed mode since the lasing inversions are created by transient conditions in the pump cycle, such as the oxygen and nitrogen lasers in the violet and ultraviolet. High-efficiency frequency doubling or even quadrupling is a practical method for obtaining radiation of shorter wave lengths. Further, many lasers can be operated in the multimode phase-locked condition, which causes the output to consist of sharp, regular spikes whose peak power may be orders of magnitude larger than the average power.

When discussing future trends during the next decade, it appears important to consider those systems which are most widely used as well as the state-of-art lasers which will probably be more restricted in use and confined to research laboratories and special projects. The more common laser oscillators, e.g., ruby (694 mμ), nd-glass (1060 mμ), he-ne (633 mμ) and argon (488 and 514.5 mμ), have already undergone intensive development, and the power capabilities, reproducibility, reliability, and efficiency have been improved enormously from earlier models. It would appear that further advance will encounter the law of diminishing returns and that an additional factor of ten in the peak power capabilities will represent an upper limit. High-power amplifiers, often using the same material as the laser oscillator, are used to obtain higher pulse energies or powers. The present limits are determined by the ability of the optical and laser materials themselves to withstand permanent damage. The molecular lasers, such as the CO_2-N_2 system, are relatively new and major advances can be expected, although the wavelengths will probably be restricted to the several micron region and longer. Because the power and efficiencies are high and the systems are comparatively inexpensive, it is expected that extensive use will be made of this type of laser.

The vast majority of transitions which are suitable for lasers are in the infrared region of the spectrum, and this condition is not likely to change. However, there is need for practical laser sources throughout the whole of the visible spectrum, and it is expected that considerable effort will be directed toward meeting this need. The widescale use of holography and photographic plates insures an increasing market for visible lasers. Also, it is more convenient to work with lasers whose radiation is visible. The he-ne 633 mμ laser will probably be a popular model for many years because of its relatively low cost, dependable operation, and long life. The output power of the majority of units will be between 1 and 100 milliwatts, although less than a milliwatt is adequate for many applications. Other CW lasers in the visible spectrum can be expected to become available, probably producing about the same power or somewhat more. The argon-ion laser will partially fill this requirement, and commercial units will probably reach the ten watt level. Frequency doubling, and even quadrupling, from 1060 mμ (nd^{3+} in yttrium-aluminum-garnet) or other infrared lasers may be a practical means for providing visible coherent sources at other wavelengths if direct lasing action throughout the visible remains difficult to achieve. Also, tunable pulsed and CW parametric oscillators and Raman lasers will almost certainly be developed.[2,3] Tunable CW parametric fluroescence has also been demonstrated,[4] and this may become an important research tool, although the power will probably be less than a microwatt.

The ruby (694 mμ) and nd-glass (1060 mμ) lasers are expected to continue to dominate the market for high-power pulsed lasers. Frequency doubling is already a practical method of obtaining shorter wavelengths from these lasers, and since the doubling efficiency is high (up to 25%), there is not a compelling need to develop new systems.

The principal laser lines are summarized in Tables 1, 2, and 3. The recent book by Smith and Sorokin[14] is also an excellent reference for details on current lasers and lasing transitions.

THE LASER PRINCIPLE

Conventional optical sources can be grouped into one of three broad classifications according to the nature of the radiation, incandescent, and emission, or line emission. Lasers have something in common with the last type of source since the active material must normally have an extremely narrow line. This line represents a transition between two energy levels in the atom, ion, or molecule. An atom which is in an excited, or upper level, tends to revert to a lower level, and the excess energy may be radiated spontaneously. This process is referred to as spontaneous emission, or fluorescence. It should be emphasized that for fluorescence to occur, it is necessary only that some of the atoms be in the upper state, and it is not required that more be in the upper than the lower level. The frequency, ν, of the emitted radiation is related to the energy difference, E, between the two levels by the Einstein relation $E = h\nu$ where h is Planck's constant.

Table 1

Principal Solid State Laser Elements Currently in use

Active Element (and Valence)	Host Lattice Material	Principal Output Wavelength
Europium (3+)	Yttrium oxide plastic chelate in alcohol	.61 μ
Chromium (3+)	Aluminum oxide	.70 μ
Samarium (2+)	Fluorides of calcium and strontium	.71 μ
Ytterbium (3+)	Glass	1.02 μ
Praseodymium (3+)	Calcium tungstate	1.05 μ
Neodymium (3+)	Various fluorides, molybdates, glass	1.06 μ
Thulium (2+)	Calcium fluoride	1.12 μ
Erbium (3+)	Calcium tungstate	1.61 μ
Thulium (3+)	Calcium tungstate, strontium fluoride	1.91 μ
Holmium (3+)	Calcium fluoride, calcium tungstate, glass	2.05 μ
Dysprosium (2+)	Calcium fluoride	2.36 μ
Uranium (3+)	Various fluorides	2.4 - 2.6 μ

Note. — The laser element may be doped into several different lattice materials in certain cases.

Table 2

Principal Gases Known to Exhibit Laser Action

Gas	Emission Distribution	Emission Frequency Range
Argon	86 lines (strong lines from 3511-5145A)	2753A - 26.95 μ
Bromine	4 lines	region of 8446 A
Carbon	9 lines	4647 A - 5.5956 μ
Cesium	2 lines	3.204 u and 8.1821 μ
Chlorine	11 lines	4781 A - 2.2060 μ
Helium	2 lines	1.9543 u and 2.0603 μ
Iodine	8 lines	5407.4 A - 3.431 μ
Krypton	59 lines	3050A - 7.0565 μ
Mercury	25 lines	4797 A - 1.813 μ
Neon	155 lines (line at 3.39 u has gain 40dB/meter)	2678.6 A - 132.8 μ
Nitrogen	9 lines	3478.7 A - 1.4547 μ

(Table continued on next page)

Table 2 - concluded

Gas	Emission Distribution	Emission Frequency Range
Oxygen	13 lines	2984.6 A - 8446.37 A
Sulfur	2 lines	1.0455 μ and 1.0636 μ
Xenon	64 lines (line at 3.507 u highest gain 60 dB/meter)	2983.8 A - 18.5 μ
Carbon monoxide	three visible bands	5590.6 A - 6613.5 μ
Carbon dioxide	two bands	9 μ and 10 μ
Deuterium Oxide	16 unidentified transitions	from 33.9 u - 107.7 μ
Nitrogen	4 bands	8683.5 A - 1.2347 μ
Ammonia (NH_2, NH_3, NH_4)	7 wavelengths	2.47 μ - 31.94 μ
Water vapor	32 unidentified transitions	
Nitrous oxide	one band	region of 10.8 μ
Hydrogen Cvanide		region of 337 microns

Note. -- With the exception of cesium vapor, all are stimulated by passage of an electrical current.

Table 3

Principal Diode Materials Currently in use in Semiconductor Lasers

Laser Diode Material	Emission Frequency Range
Gallium arsenide	0.840 μ - 0.932 μ
Indium phosphide	0.900 μ - 0.919 μ
Indium arsenide	3.112 μ
Gallium indium-arsenide	0.840 μ - 3.100 μ
Indium antimonide	5.200 μ
Gallium arsenide-phosphide	0.610 μ - 0.840 μ

Note. — Efficiency of operation is high approaching 40%; however, total power density that can be achieved is low.

If a material shows a strong emission line in fluorescence, it is also found to be a strong absorber of radiation of the same wavelength. When absorption occurs the atom is raised from the lower to the upper state, or it may be said that the atom is stimulated to a higher level. A corresponding process in emission also occurs; atoms in the upper state can be stimulated to emit radiation and, in the process, drop to the lower level. It should be emphasized that the stimulation process is basically different from the spontaneous process, since the former occurs in either direction (absorption or emission) while the latter occurs only in emission. Absorption and stimulated emission are fundamentally the same process, and both occur simultaneously whenever radiation of the resonant wavelength passes through the material. Which process is dominant depends on the relative number of atoms in the two levels: if more are in the higher level, there is net emission; while if more are in the lower state, there is net absorption. Normally the lower state has the larger population and absorption occurs. When the upper state can be made to have the larger population, the material has gain and is a possible source for laser action. This condition is comparatively difficult to achieve, and the material is said to have an inverted population.

To further illustrate the laser principle, consider a flame to which a small amount of salt is added in order to produce the yellow lines of sodium in fluorescence. If a narrow beam of radiation at the same wavelength as one of the sodium lines is passed through the flame, the radiation is slightly absorbed. In order to have laser action, it would be necessary for the yellow flame to cause an increase in the intensity of the narrow beam as it passed through. To produce laser action, it is required that the population of the two levels be inverted so that the material amplifies its own spontaneous emission.

To achieve an inverted population, the upper level must have a relatively long lifetime, and it is necessary to pump or excite the atom into this state. The commonest means of pumping a solid state laser is by means of intense light from a flashlamp. For gas lasers, a discharge is set up by means of an rf or dc excitation. In semiconductor lasers, a large dc current is passed through the junction.

A laser material amplifies by means of stimulated emission, but does not constitute an oscillator unless a resonator is provided. The simplest form of resonator consists of two flat mirrors which are made parallel and positioned one on either side of the active material so as to intercept as much of the stimulated emission as possible. The same conditions hold for an optical frequency oscillator as for one at lower frequency; if the gain of the laser material is sufficient to overcome losses, the system will oscillate at one of the natural frequencies of the system. The amplitude of the oscillation increases until saturation effects cause the gain to become equal to loss. Multiple-layer dielectric coatings can be produced with losses as low as a few tenths of a percent, so that even low gain transitions can be made to oscillate. Although flat mirrors are still used in most solid state lasers, concave spherical reflectors are more common in gas lasers since the tilt of the mirrors does not have to be adjusted as accurately.

The frequency separation between the primary resonator modes is approximately c/2L where L is the length of the cavity and c is the velocity of light. For a one-meter resonator, the separation is 1.5 X 10^8 cycles per second, or 0.005 cm^{-1}. The linewidth of most laser materials is considerably greater than this, so that lasers tend to have several modes oscillating simultaneously. The presence of several independent modes is not of major significance in most applications except that the amplitude noise is high. However, it is possible for the modes to become coupled together so that they are phase-locked to one another and produce intense spikes in the output.[5,6,7,8] Even when many modes are present, the radiation is highly monochromatic by most standards. For he-ne (633 mμ) the linewidth is about 1.5 X 10^9 cycles per second, which can be expressed as 0.05 cm^{-1} or as 0.02 Angstroms.

CHARACTERISTICS OF LASER RADIATION

The most important characteristic of laser radiation is its excellent coherence, both in time and space. That is, the emission is highly monochromatic and can be focused to an extremely small beam area.

The linewidth of a single mode he-ne laser is determined by mirror vibration and is of the order of 10^5 cycles/second, or 10^{-6} Angstroms, under good laboratory conditions. However, most lasers have many modes present, and the total frequency spread is primarily determined by the width of the fluorescent line of the active material, as discussed briefly in the previous section. Except for nd-glass, the linewidths of most of the common lasers are still very narrow even when oscillating multimode. For example, the use of a resonant reflector in a ruby laser will limit the frequency spread to about 10^9 cycles per second, or 0.02 Angstroms.

The excellent spatial coherence of most lasers results from the use of a resonator with highly precise mirror surfaces. The wavefront of the beam radiated from the output mirror matches the shape of the mirror surface and is, therefore, a plane-wave if the mirror is flat, and a spherical wave if the mirror is curved. In some instances, the active material introduces significant wavefront distortion because of optical inhomogeneities, and the presence of off-axial modes is a further complication. However, it has been reported that in the best of ruby lasers under ideal conditions the beam divergence can approach the diffraction limit.

The practical effect of good spatial coherence is that when a positive lens is placed in the beam, the size of the focal spot, or image, is extremely small, and for some lasers the diameter of the spot focused by a perfect lens is limited only by diffraction. As long as lens aberrations do not become significant, the larger the diameter of the parallel beam as it enters the lens, the smaller the size of the focal spot, so that even from medium power CW laser, it is possible to obtain extremely high power density over this very small area. The giant pulse lasers have intensities of the order of 10^9 watts per cm^2 even when unfocused, so that it is not surprising that a focused beam can shatter crystals or generate a spark.

It is interesting to compare the intensity of the sun's image at the focal point of a lens with that of a medium power he-ne visible laser. Assume an f/4 lens, with a focal length of the 10 cm and a diameter of 2.5 cm. The sun subtends an angle of about 0.01 radians, so that the diameter of the image is one millimeter. The intensity of the sun's radiation is about 100 milliwatts per cm^2, so that at the focal point the power density is approximately 50 watts per cm^2. If the laser beam is 3 millimeters in diameter and the laser is generating only longitudinal modes with no transverse modes, the angular width of the central lobe of the diffraction pattern is approximately given by λ/d radians, when λ is the wavelength, and d is the diameter of the beam. The diameter of the focal spot is approximately $10\lambda/d$, since the focal length is 10 cm. This gives a diameter of about 20 microns. If the output power of the laser is 50 milliwatts, the intensity at the focus is approximately 1.6×10^4 watts per cm^2.

SOLID STATE LASERS

The laser rod or crystal is situated in a reflecting chamber along with a pump source (usually a flash lamp). Electrical power stored in a capacitor bank is suddenly discharged through the flash lamp. Some of the light is absorbed in the laser rod and excites the atoms or ions (cr^{3+} ions in the case of ruby) from the ground state to an excited level. In ruby, there is then a very rapid transition to the upper laser level, and laser action occurs to the ground state. Ruby is an example of a three-level system.

The laser resonator may consist of the rod itself, in which case one end is coated so as to reflect most of the energy (99%) and the other end is partially transmitting. In other cases, the rod is placed between separate mirrors.

Other types of solid state lasers, such as those containing neodymium, function at four energy levels. In these crystals, the terminal laser level is above that of the ground state far enough so that it is normally nearly empty at the operating temperature of the laser, thus reducing pumping power requirements. In addition, the pump bands absorbed by neodymium are much wider than for most similar crystals and pumping can also be accomplished to several upper energy states rather than one or two narrow bands as is the case with ruby. While there are three principal lines for emission from this material, over 98% of the emitted energy lies at the wavelength of 1060 mμ. As energy outputs increase, it may be expected that the total amount of energy available in the lesser lines will also increase proportionately.

Solid state lasers most used to date include the following: (a) ruby, which is chromium (3+) substitutionally replacing aluminum in aluminum oxide, (b) neodymium (3+) in crown glass or in various fluorides, calcium tungstate, or yttrium aluminum garnet (YAG), (c) europium (3+) in yttrium oxide, and (d) uranium (3+) in various fluorides. These and others of importance are listed in Table 1.

Wavelengths achieved from solid state lasers have varied between 610 mμ for europium and 2600 mμ for uranium. Energy outputs using neodymium in glass have gone up into the thousands of joules per pulse with repetition rates as high as 5 to 10 per minute. Most biologic work has been done with crystals doped with chromium and neodymium.

GAS LASERS

The first gas laser was built by Javan, Bennett and Herriott in 1961[9]. It gave a continuous output of one milliwatt at several wavelengths near one micron with the principal emission at 1150 mμ. The gases used were helium and neon. While much work with lasers has been done using these gases, at present more than 500 lines are known to exhibit laser action under either continuous or pulsed excitation. Wavelengths from gas lasers range from the ultraviolet (neon-268 mμ) into the infrared (HCN-337 microns), and they may be pulsed, continuous, or quasi-continuous. The helium-neon combination, just as most of the others, can give coherent laser output at many wavelength including several in the visibile portion of the spectrum. Using certain reflector techniques, various spectral regions can be selected. The strongest visible laser line from the helium-neon mixture is at 633 mμ. Recently, considerable work has been done using carbon dioxide and nitrogen, and also ionized rare gas lasers. Relatively high powers have been achieved from these devices with outputs reported in the 20 watt range for ionized argon and over 1,000 watts for carbon dioxide. Table 2 lists those gases which have demonstrated laser action together with the wavelengths achieved. Although most emit a large number of lines, tuning techniques may be used to select the desired wavelength.

Gas lasers are usually operated as continuous (CW) sources, and have a beam divergence close to the theoretical minimum. Although most gas lasers have several modes present they can be operated so as to produce only a single mode.

Most gas lasers are four-level systems. Population inversion is maintained between two upper excited levels, which can be labelled E_3 and E_2. The upper level, E_3, undergoes stimulated emission to the lower state, E_2. Depopulation of E_2 occurs by spontaneous emission to an intermediate metastable state, E_1, rather than to the ground state, E_0, from whence repumping to E_3 can be accomplished. The fact that E_1 is metastable hinders the decay of this state and its return to E_0. Thus, population inversion density versus pumping rate can saturate or even decrease due not only to resonance trapping at the lower metastable level but also to electron re-excitation from that level. This so-called metastable "bottleneck" has prevented most gas lasers from achieving higher power outputs or more efficient operating conditions.

The ionized gas laser seems to be the first step in overcoming this metastable drawback. In the ion laser, the contained gas is ionized by passage of an electrical current and the active laser material consists of excited ions. Excitation then occurs principally by electron impact with ground state neutral atoms. Although efficiency is low, less than 1%, no distinct saturation limit on pumping rate relative to power output has been observed.

Another class of lasers has been proposed called "collision" lasers. In collision lasers the metastable problem can be overcome by using various atomic collision processes against one another so as to cause depopulation of the metastable level to the ground state. Using these devices, 50% efficiency is not an unreasonable figure to consider attainable.

More recently energy levels of the vibration-rotation spectrum of carbon dioxide have been used to achieve continuous outputs at high powers (1,000 watts has been reported). In the operation of this device, a dc discharge directly into a mixture of carbon dioxide and nitrogen-helium results in the excitation of large numbers of nitrogen molecules to a vibrational energy level almost identical with an energy level for carbon dioxide. A selective transfer of energy to carbon dioxide molecules occurs with population inversion being thereby accomplished.

Since the vibrational level of nitrogen has a relatively long lifetime, the pumping mechanism is extremely efficient, about 14%. While other gases have been used in place of carbon dioxide, i.e., nitrous oxide, carbon monoxide, and carbon disulfide, highest power outputs have been achieved using the former.

SEMICONDUCTOR LASERS

In November 1962, successful laser action was first achieved in the junction region of a gallium arsenide semiconductor diode[10, 11, 12]. Since that time, laser action has been achieved in gallium arsenide-phosphide, indium arsenide, indium phosphide, gallium indium-arsenide, and indium antimonide at wavelengths ranging from 0.65 microns to 5.2 microns. The wavelength range has been extended to 22 microns using lead sulfide, lead telluride, and lead selenide. Principal diodes currently in use are listed in Table 3.

If an electrical forward bias is applied to a semiconductor diode, electrons enter the junction region and occupy energetic states near or within the conduction band. Simultaneously, electron vacancies in less energetic states near or within the valence band appear in the diode junction. Radiation occurs as electrons pass this junction and make the transition back to the valence band from the conduction band. When the junction current is large enough, there will be more electrons near the edge of the conduction band than at the edge of the valence band and a population inversion may occur. Under these conditions, and utilizing crystals such as gallium arsenide that have been properly made, laser action will occur thoughout the junction region. Useful laser emission is obtained at the semiconductor-air interface at the edge of the junction.

Internal ohmic loss in the diode is the principal problem associated with obtaining high peak power pulses from most semiconductor or injection lasers for current pulses of less than 1 microsecond duration. Raising the temperature of a laser diode tends to increase the current density necessary for threshold. At 20°K GaAs diodes have been reported to yield 6 watts of continuous power and at 80°K power in excess of 1 watt has been obtained under CW conditions. Room temperature pulsed operation of GaAs has produced 60 watts of peak power in 100 microsecond pulses at 30 cycles per second. At lower temperatures, several hundred watts of peak pulse power are available from GaAs. Total energy delivered per pulse, however, has been small.

At room temperature, laser emission from pure GaAs occurs at a wavelength of about 900 mμ. At lower temperatures the output wavelength decreases to about 840 mμ. The output can therefore be tuned over a considerable range simply by varying the temperature. Still further change in wavelength can be achieved by using a three-element alloy mixture such as gallium arsenide phosphide. Depending on the ratio of arsenic to phosphorus, such a diode will operate between 610 mμ and 840 mμ. A three-element mixture of gallium indium arsenide shows promise of operating from 0.84 to 3.1 microns. By adjusting the temperature of operation, the output can be brought close to any wavelength desired. While it is difficult to achieve an accurately reproducible wavelength, diode lasers have the advantages of compactness, simplicity, increased efficiency of operation, a power output that may be adjusted and quickly controlled by simply changing the electrical input into the diode.

SPECIAL SYSTEMS

Gaint pulse laser

Using special techniques it is possible to achieve enormously high peak powers in very short pulses. This method is called gaint pulsing, or Q-switching, and is accomplished by interposing a fast action shutter between one end of the laser rod and the mirror. During most of the pumping cycle, the shutter is closed so that the Q of the resonant cavity is low, i.e., the losses are high, since light from the end of the rod cannot reach the mirror and be reflected back. Therefore, since the gain does not exceed the losses, laser oscillations cannot start even though a large number of atoms are in the excited state and the gain is high. When the laser element has been pumped sufficiently, the shutter is opened quickly. This restores the high Q of the resonant cavity and the oscillations build up very rapidly. Under these conditions, the stored energy is delivered in one giant pulse, and peak powers as high as a few gigawatts have been achieved. The pulse width is extremely short, usually lasting for only 5 to 30 nanoseconds (1 nanosecond = 10^{-9} second). Devices currently in use for Q-switching include electro-optical shutters, rapidly rotating mirrors, rotating prisms, bleachable absorbers, and various combinations of these.

It should be emphasized that even though very high peak powers are obtained, the pulses are short and the total amount of energy delivered is small, rarely exceeding a few joules.

Raman effect

When a laser beam is passed into certain liquids such as benzene or nitrobenzene, additional coherent, well-collimated wavelengths are propagated out of the liquid. These new wavelengths result from frequency shifts of the original wavelength by multiples of the various molecular vibrational frequencies of the liquid through which the laser beam is passed. Such a shift is called the "Raman effect". While most of these frequency shifts are downwards (Stokes lines), under certain conditions upward shifts may occur (anti-Stokes lines).

If a chamber containing the liquid being irradiated is placed between two parallel end mirrors so as to form a light resonating cavity, laser light oscillation and amplification will occur at either one or more of the Stokes frequencies, depending on whether or not oscillation threshold for the particular line is reached.

Discovery of the stimulated Raman effect using laser beams has made available many new wavelengths of high intensity coherent light.

Harmonic generation

Because of the intense power density which can be obtained in focused laser beams, and in particular with giant pulse lasers, it is possible to generate appreciable harmonic power in many materials. All substances, presumably, are nonlinear when the intensity of the radiation is sufficiently high, but a few crystals are particularly effective in generating harmonics. The most widely used materials for second harmonic generation are potassium dihydrogen phosphate (KDP), ammonium dihydrogen phosphate (ADP) and lithium niobate ($LiNbO_3$).

A small amount of harmonic field is generated as the laser beam traverses the crystal. In order for the efficiency of conversion to be significant, it is necessary for the harmonic and fundamental waves to travel with the same velocity so that the harmonic generation is cumulative. Because of dispersion in the index of refraction, the wave velocity changes with wavelength, and velocity matching, or phase matching, is normally not obtained. However, phase matching is possible in birefringent crystals. For example, in $LiNbO_3$ the laser can be transmitted as an ordinary wave (o-wave) and the second harmonic as an extraordinary wave (e-wave).

By rotation of the crystal axes or by changing the temperature of the crystal, the two velocities can be made equal. Lithium niobate is particularly useful for generating second harmonic from a laser which is operating at about 1000 mμ, while KDP and ADP are used for wavelengths of the fundamental from about 1000 mμ to 500 mμ.

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CHAPTER II

RETINAL INJURY FROM LASERS AND OTHER LIGHT SOURCES

Walter J. Geeraets*

The purpose of this report is the review and discussion of some of the findings presented in the literature relating to permanent injury to the eye caused by laser irradiation and light coagulation. Since this study is concerned with our present knowledge of retinal energy doses capable of producing permanent injury, only those studies are summarized and discussed which give data on exposure times, image sizes of the irradiating beam on the retina, and energy levels.

A point which must be stressed is the definition of "retinal threshold lesions". Since the introduction of the term "retinal threshold lesions" by Ham _et al_.[1] a number of misunderstandings regarding this concept have occurred, both in the literature and in the minds of investigators concerned with the problem of retinal injury. The original definition of a threshold lesion as an ophthalmoscopically observable lesion barely visible five minutes after exposure was based on probit analysis of RD-50 data[1]. A burn of this type may be termed "threshold" or "minimal" only in the sense that it fits this particular definition, but it may not be threshold or minimal by other criteria or examination procedures[2]. During recent years it has been shown that irreversible damage at lower levels of irradiance can be demonstrated by more refined techniques, such as histochemistry[2], electroretinography[3], and others[4]. In addition, irreversible lesions can appear at lower irradiance when the observation time is extended to several days after exposure[5-7].

In this report the amount of energy required for the production of minimal ophthalmoscopic visible lesions is given as retinal irradiance (watts/cm^2) or retinal dose (j/cm^2). Presenting the "threshold" irradiances or doses for various wavelengths and exposure times for energy incident on the retina, rather than on the cornea, has the advantage that certain physical considerations such as pupillary diameter, transmission co-efficient of the ocular media, and spectral absorption characteristics of the retina and choroid are already incorporated into these data. Therefore, in a given situation the energy density on the cornea has to be determined, and from this measurement the retinal irradiance can easily be calculated by using the equation:

$$\frac{\phi_r = \phi_c \times D^2 \times k = \text{watts/cm}^2}{d^2}$$

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ϕ_r = retinal irradiance (watts/cm^2)

ϕ_c = corneal irradiance (watts/cm^2)

D = pupillary diameter

k = average transmission coefficient through the ocular media for a given spectral distribution or wavelength.

d = diameter of the image on the retina, depending on the divergence of the incident beam of light and the focal length of the eye (for the normal emmetropic human eye approximately 0.3 mm/1° bean divergence).

INTRODUCTION

Thermal injury to the retina has been known for many centuries. As early as 200-130 A.D., Galen described eclipse blindness[8]. Galilieo received ocular injury by watching the sun through his telescope[9]. In this century, a great number of people received retinal burns during the solar eclipse in 1912[10]. However, the first scientific description of thermal injury to the eye was reported by Verhoeff and Bell 1916[11]. These investigators pointed out that eclipse burns were actually thermal lesions, originating in the retinal pigment epithelium by the transfer of light energy to heat. During World War II, numerous foveal lesions were documented among persons using optical instrumentation to "spot" planes attacking from the direction of the sun[12].

With the development of nuclear weapons another source capable of producing retinal injury was introduced. In 1953 Buettner and Rose[13] pointed to this potential hazard to the eye and brought attention to the focal properties of the eye which compensates for the "inverse square law" of attenuation out to distances where the spot size of the fireball on the retina is limited by diffraction. The field conditions were simulated in the laboratory by Ham *et al.*[1], who used an army search light as the power source, and by the extensive work of a group of investigators of the USAF School of Aerospace Medicine, Brooks AFB, Texas[14].

On the basis of the effects of eclipse burns on the human retina, Meyer-Schwickerath[15] began experiments with high power light sources to develop "clinical light coagulation" for the treatment of certain ocular pathologies. During this development he first used the sun itself as the light source. This was followed by a carbon arc lamp and finally, in collaboration with Littman, he developed the Xenon high pressure lamp coagulator, which has become well known as the "Zeiss light coagulator". The first clinical light coagulation of a retinal lesion was performed in this country by Guerry in 1958[16] using the experimental instrumentation of Ham *et. al.*[1].

With the advancement in research and development of lasers, a new source of radiation has become available which presents great potential hazard to the eye if the proper protective mechanisms are not used. After the development of the first successful optical laser in 1954 by Gordon, Zeiger, and Townes[17] of Columbia University, Maiman[18], succeeded in the development of the ruby solid state laser in 1959. Since then, enormous progress has been made in the advancement of laser technology. Today, coherent electromagnetic radiation by simulated emission extends spectrally from the ultraviolet to the far infrared utilizing solid state lasers, liquid lasers, and gaseous lasers. The power of these devices ranges from milliwatts to gigawatts (see section I). They may be operated as pulsed lasers, ranging from few nanoseconds to several milliseconds, or they may produce continuous radiation (CW). Their unique properties lie in their directionality, monochromaticity, coherency, and polarization.

OCULAR SPECTRAL CHARACTERISTICS

Ocular transmission. The production of thermal lesions in the ocular fundus depends, among other factors, upon the spectral quality of the light incident on the cornea and the spectral characteristics of the eye itself. In previous articles[19-25] the spectral characteristics of the eye have been described. The spectral range over which transmission studies had been performed varied with the various investigators but generally included the visible portion. The early work of Ludvigh and McCarthy[19] was hampered by lack of more refined and modern instrumentation and gives much lower transmission coefficients than those reported by Kinsey[20] and Geeraets and coworkers[24,25]. It is more difficult to account for the discrepancy between the latter results and those given by Prince[22], Wiesinger, et al.[21] have shown that there is little difference between their transmission values for rabbit ocular media and that for a 1 cm thickness of physiological saline.

To estimate retinal injury by light exposure, absorption data for retina and choroid are best given for energy incident on the cornea. Previous reported absorption values for the human retinal pigment epithelium and choroid include light scattered and reflected by the various structures of the eye[24,25]. This resulted in excessively high absorption values. Though this fact lets one be on the safe side when estimating retinal hazards, correction of these data for reflection seemed to be desirable. More recently completed work[26] has resulted in such corrected absorption characteristics (Figs. 1-3).

The influence of blood upon ocular spectral absorption has been discussed in previous communications[25] and in vivo reflection measurements allowed an estimation of retinal thermal injury[27].

The energy density gradiant in the fundus depends upon the concentration of the pigment within the granules and the space distribution of the pigment granules within a given cell and cell layer. The

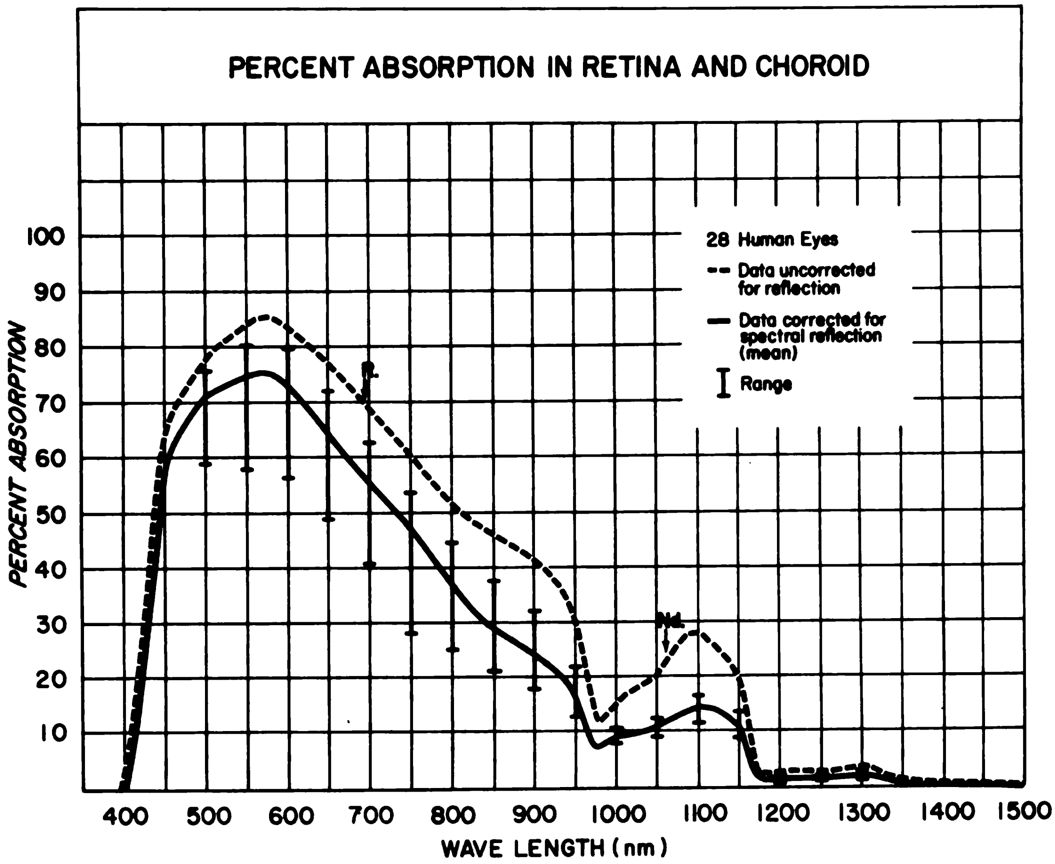

Figure 1. Percent absorption in retinal pigment epithelium and choroid for equal intensities and light incident on the cornea. (Human data) R = Ruby laser wavelength. ND = Neodynium laser wavelength.

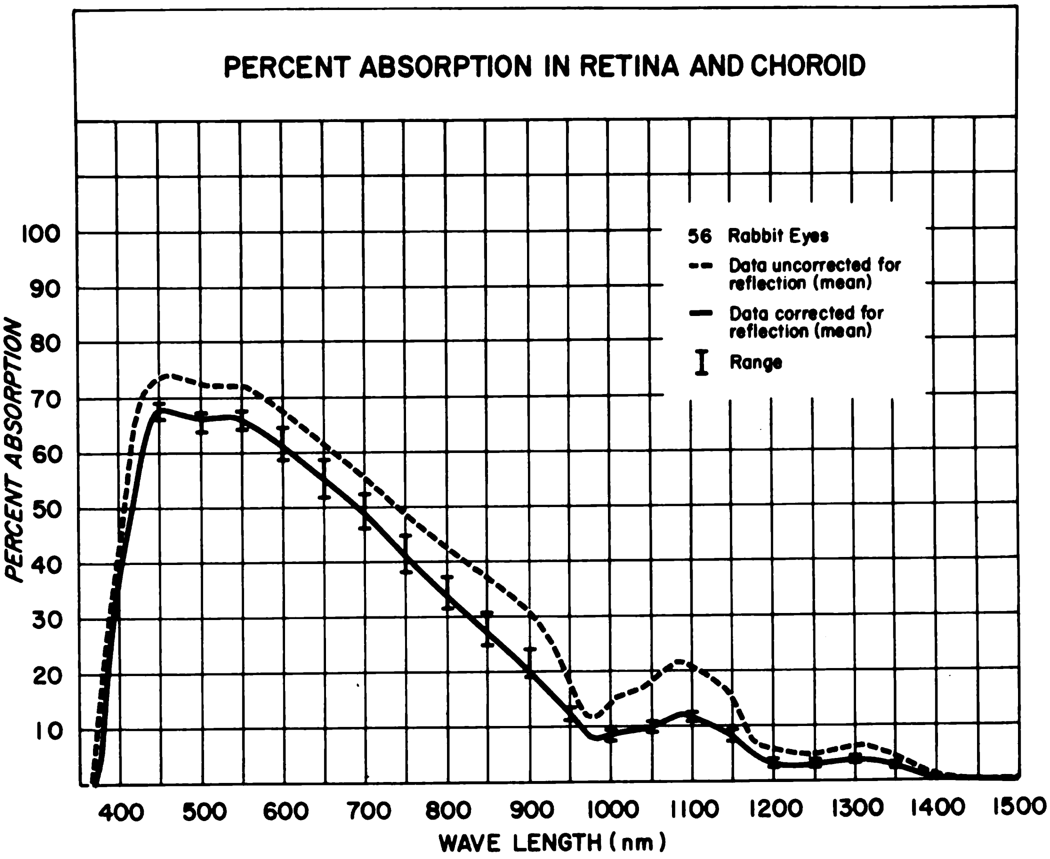

Figure 2. Percent absorption in retinal pigment epithelium and choroid for equal intensities and light incident on the cornea. (Rabbit data) R = Ruby laser wavelength. ND = Neodynium laser wavelength.

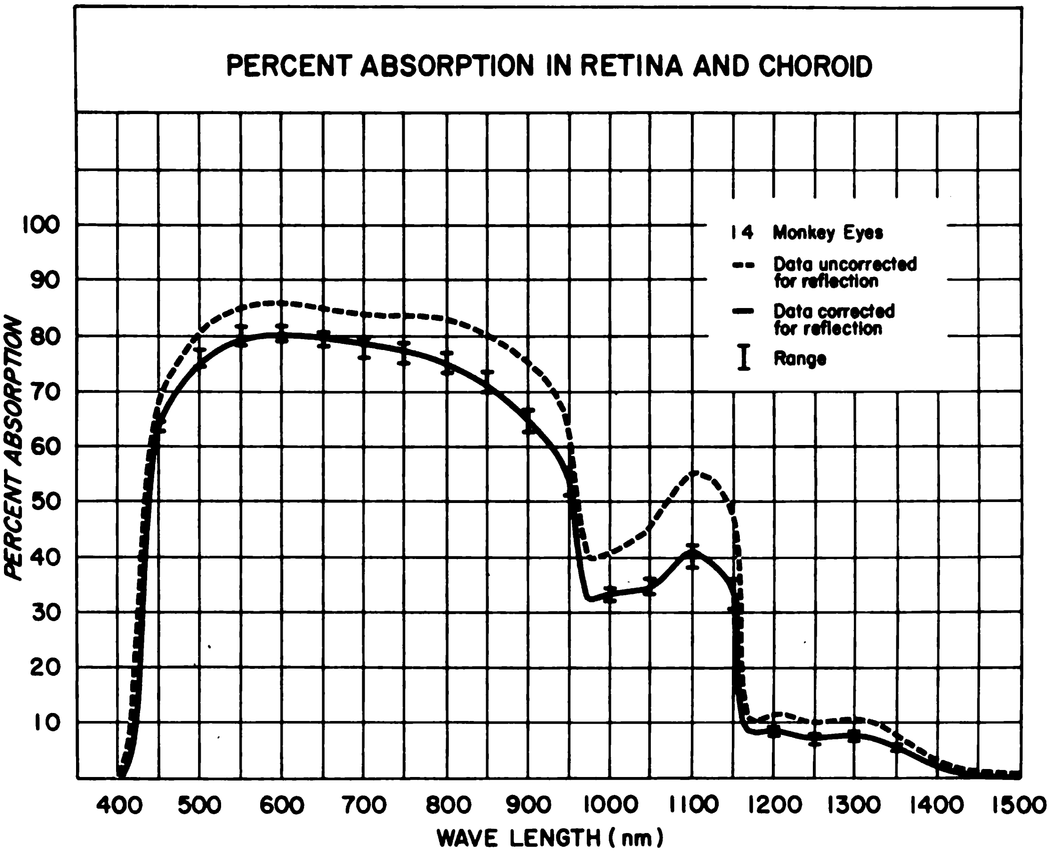

Figure 3. Percent absorption in retinal pigment epithelium and choroid for equal intensities and light incident on the cornea. (Rhesus monkey data) R = Ruby laser wavelength. ND = Neodynium laser wavelength.

distribution of pigment granules varies in both pigment epithelium and choroid but more markedly in the latter. Absorption of radiant energy in human and rabbit pigment epithelium may be greater than in the choroid, or vice versa, depending on the individual.

Though the pigment density may vary from one area to another in one and the same eye, an even greater variation of pigment density exists from one species to the other. It is for this reason that in previous investigations mainly chinchilla rabbits were used to study the thermal effect on retina and choroid with the intention of finding a suitable model for the human fundus. It should be stressed that the rabbit eye in its anatomy and optics is quite different from the human eye (i.e. the absence of a foveal region in the rabbit eye and the lack of retinal vascularization). However, the transmission and absorption characteristics of the ocular fundus, particularly the retinal pigment epithelium and the choroid, are very similar in the rabbit and human. On the other hand, the anatomical and optical characteristics of the eye of the Rhesus monkey are quite similar to the human eye; the foveal region and retinal vascularization are similar to the human eye. However, at long exposure times and/or at energy levels greater than that required for the production of minimal retinal injury, the more intense choroidal pigmentation of the Rhesus eye contributes markedly to the development of retinal thermal lesions. It is for these reasons that data obtained in the Rhesus monkey eyes require cautions when correlating human ocular hazard from light exposure. Zaret and co-workers [28] in their studies have used the Douroucouli monkey, and according to these investigators the retinal and choroidal pigment density and distribution in this animal are very similar to the human eye.

<u>Ocular spectral reflectance</u>. Preliminary spectral reflectance measurements have been made on human, Rhesus monkey, dutch and chinchilla rabbit eyes [26]. The measurements were taken from 350 nm through 1500 nm with the neural retina still attached to the retinal pigment epithelium and were repeated with the neural retina removed. The earlier reported values for absorption in retinal pigment epithelium and choroid [24,25] were corrected for these reflection data. The new absorption data thus more closely represent true absorption and give a more accurate estimate of absorbed energy at individual wavelength (Figs. 1-3).

OPHTHALMOSCOPIC FINDINGS IN MINIMAL RETINAL INJURY

The ophthalmoscopic visible findings for minimal retinal injury can be grouped in three sub-divisions: 1) for long exposure times (ms to sec.), 2) for short exposure times (us to ms ranges), and 3) q-switched laser lesions (ns ranges).

Lesions in the fundus of the human, monkey, or rabbit eye can be described collectively since their gross ophthalmoscopic appearance is so similar that small deviations in the different species may be neglected. When the exposure time is varied, however, the lesion produced have characteristic differences.

Lesions Produced With Long Exposure Times.

Minimal retinal lesions produced at long exposure times, approximately 30 ms to 300 ms, are usually smaller than the actual image size of the light beam on the retina. This feature can be explained by phenomena of heat conduction. The thermal flux at the periphery of the irradiated field causes a notably smaller temperature rise, one inadequate for producing thermal injury. The clinical picture of such a lesion is characterized by slightly darker discoloration of the fundus under observation with red free light. Usually the edges of these lesions are somewhat blurred.

With slightly higher intensity the lesion becomes greyish, usually with a pearly white center and a peripheral zone of retinal edema. A small orange-colored halo then ensures, fading out peripherally in a zone of darker reddish color possibly due to hyperemia of the choroidal vessels. Due to thermal conduction in the periphery the size of these lesions might be larger than the image size of the light beam.

Heavy lesions show eventually chorio-retinal rupture in the center of the exposed field and possible preretinal or vitreous hemorrhages in the center of the lesion. Such explosive chorio-retinal lesions are produced with energies many times greater than those required for production of mild retinal lesions. They are always larger than the retinal image size of the light beam. Subretinal hemorrhages are usually not observed at this long exposure time for heat general causes early coagulation of the adjacent structures as well as of choroidal vessels, thus preventing the spread of choroidal and subretinal hemorrhages.

Lesions Produced at Microsecond and Millisecond Ranges.

In this range of exposure times, retinal lesions have a similar appearance whether they are produced with the Xenon high pressure light coagulator or with a laser with an emission within the visible spectrum. These lesions appear somewhat different from those produced at long exposure times. Minimal lesions usually present slightly darker coloration than the surrounding fundus and moderate to severe lesions show a uniform, greyish area. For minimal and above minimal lesions the size of the lesion is approximately equal to the image size of the exposure light beam or laser beam. This might indicate that the effect of heat conduction is minimal during short exposure times (i.e. within this exposure range). This effect of minimal spreading of cellular injury peripherally to the boundary of the irradiated area has been confirmed and demonstrated in histochemical and other studies[2,35].

Moderate lesions show a rather unifrom grey appearance with a pale, narrow halo surrounding it, while very heavy lesions often present centrally located pigment accumulation and hemorrhages, either intraretinal or preretinal. This ia a common feature for rather heavy lesions produced with both white light or laser exposures. The center of the lesion with the hemorrhage and pigment accumulation is mostly surrounded by a snow white area borderlined by a small cuff of irregular pigment distribution. Coagulation apparently prevents subretinal spreading of hemorrhages, for this usually does not occur.

Q-switched Laser Lesions in Nanosecond Ranges.

Retinal lesions produced at extremely short exposure times present a characteristic feature different from the one described in microseconds or milliseconds. Very minimal lesions appear as small dark reddish areas. They usually change to a mild or greyish appearance after several minutes. This phenomenon can particularly be well observed by red free light. Very minimal lesions usually do not demonstrate any intraretinal or subretinal hemorrhages; however, there is frequently a slight pigment irregularity observable within the irradiated area. After several days this becomes more pronounced with irregularly distributed pigmentation. If the energy dose is slightly increased, subretinal and intraretinal hemorrhages occur that frequently spread slowly, separating the neural retinal layer from the pigment epithelium. In severe lesions, intraretinal and preretinal hemorrhages become pronounced, sometimes following channel formation through the retina and into the vitreous. This appearance has been explained by the discharge of pigment clumps from the pigment epithelium through the neural retina into the vitreous. Along their course, hemorrhages originating from the choroidal capillary layer follow these channels and give this strange appearance. The surrounding retina is usually greyish white and widespread subretinal and choroidal hemorrhages are associated with these lesions. This particular clinical feature leads to assume that a "typical" thermal coagulation effect during or after irradiation is absent. The total diameter of these lesions is determined by the extent of the subretinal hemorrhages.

HISTOLOGICAL FINDINGS

Histological description of the produced lesions, either by light coagulation or various laser coagulations, is subdivided into the same three groups as the clinical observations: long exposures, intermediate exposures, and short exposures. Since the histological alterations after exposures are very similar for different species (human, Rhesus monkey, and rabbit), typical histopathological changes after irradiation are described for these three species together.

It should be understood that the similarities of the lesion are mainly in the range of minimal or so-called threshold lesions, since for the production of these minimal lesions, apparently only the retinal pigment epithelium is primarily involved. For longer exposure times or more intense lesions (which means an increase in energy or power density), the choroidal pigmentation plays a significant role, and therefore, the histopathological feature of the produced chorioretinal lesion varies depending on the amount and distribution of pigmented cells.

Long Exposure Times (30-300 ms).

For long exposure times, the histological findings have been described by many investigators. Meyer-Schwickerath [15] gave an excellent presentation of the histological changes after light coagulation with the Xenon high pressure lamp. The characteristic features for mild lesions are a narrowing of the receptor cell layer and an increased susceptibility for certain stains such as eosin and periodic acid Schiff reaction (PAS). Both stainings, because of their apparently higher affinity for coagulated tissue, represent in a moderate way an indicator for detection of minimal retinal thermal injury. Probably somewhat more pronounced and more sensitive is alcian blue for acid mucopolysaccharides, which are present in higher concentration between the outer segments of the receptor cells. Also the pentachrome stain seems to show more intense staining in the areas of thermal damage. Nitro BT tetrazolium studies for cytochemical localization of oxidative enzyme systems represent another useful method [2].

At long exposure times, minimal lesions already show definite adherence to the underlying retinal pigment epithelium which becomes very obvious during sectioning and preparation of the histological material, for otherwise the neural retinal layers become easily detached during processing of the histological specimen. In addition one can see even in mild lesions, that the nuclei of the outer and inner nuclear layers become somewhat less sharply defined. There seems to be a certain "loosening" between the nuclei, with interspaces, and there is a darker staining with hematoxylin. Mild edema is frequently present in the inner retinal layers. In moderate lesions the outer nuclear layer is often in this layer. However, the most likely one might be that in moderate lesions the coagulation effect of the proteins causes tight adherence of the coagulated outer layers of the retina and pigmented structures of the eye, whereas severe edema occurs in the most vulnerable layers of the retina, the nuclear layers, with regard to structural stability with resulting spatial disruption of the cellular elements.

If the energy is further increased, all inner layers of the retina are involved, and the severe coagulation effect coexists with disruption and distortion of the normal anatomical architecture. The choroid usually shows hyperemia and thickening with pyknosis of the nuclei, a feature which may be seen in the sclera as well.

Intermediate Exposure Times (microsecond to millisecond ranges).

Very mild lesions show minimal changes in the retinal pigment epithelium and the receptor cell layer only. There may be some vacuolization in the PE cells, and the receptor organs often seem more adherent with increased staining of affinity to various stains. At slightly higher energy levels there is some darker staining of the nuclei in the outer nuclear layer and loosening of the pigment epithelial cells. This feature is very characteristic and is seen after exposures with the Xenon light coagulator as well as with a normal pulsed ruby laser.

A similar affinity to certain histological stains as mentioned for lesions produced at relative long exposure times has also been reported for those produced with ruby laser at 500 μs [29]. Shuman and Maloney [30] examined laser exposed retinae by phosphotungstic acid hematoxylin and PAS techniques as well as by naphthol ASTR acid phophatase and nitro BT tetrazolium succinic oxidase cryostate methods. While they observed an increase in staining affinity for PAS and ASTR and a marked decrease in PTAH, 24 hours after exposure formazan deposition showed only minimal change. These authors concluded from their observations that non-thermal components of the interaction could be postulated since they did not observe injury of the pigment cells with their method.

If the energy is increased above that which results in minimal lesions, the diameter of the lesion does not increase as markedly as it does with the longer exposure times. The involvement of the choroid is markedly less and no scleral changes are demonstrable by ordinary histological techniques. The histological changes seem to be more confined to the outer layers of the retina and with less involvement of the inner layers of neural retina. Hemorrhages into the retina or choroid are not observed in moderate injury inflicted at these exposure times.

If the energy is increased still further, disruption of pigment epithelial cells occurs with dislodging of pigment granules. These granules are dispersed through neighboring retinal pigment epithelial cells and throughout the outer segment of the retinal receptor cells. Choroidal and intraretinal hemorrhages may occur. The extent of damage to the inner retinal layers is proportional to the power density incident on the retina.

At high irradiances disruption of choroid and retina will ensue with resulting hemorrhages in these structures which may extend into the vitreous.

Q-Switched Ruby Laser Effect (nanosecond ranges).

At this very short exposure time two outstanding features are present: 1) there seems to be no adherent effect between the outer retinal layers and the pigment epithelium, and 2) there seems to be, even in minimal lesions, displacement of pigment epithelium cells and pigment granules anteriorly. Usually there is slight swelling of the outer segment of the receptor cell layer. The remaining neural layers of the more inner retinal structures seem to be undisturbed. The displacement of the retinal pigment epithelium anteriorly, increases with increasing intensity of the incident flash. Even at slight increases of the power density, hemorrhages deriving from the chorio-capillaries prevail and are usually seen as small aggregates of red blood cells between the PE layer and the receptor cell layer. The PE cells in these areas are disrupted, and the rods and cones show swelling and distortion.

In moderate lesions, disruption of pigment epithelium cells is always present and pronounced, with retinal pigment granules throughout the outer and inner retinal layers. Fractions of choroidal tissue are frequently found, displaced forward into the subretinal space along with profuse hemorrhages. Subretinal and intraretinal hemorrhages are evident, though the retinal architecture is normally well recognizable.

If the energy density is further increased, explosion-like disruption takes place with discharge of accumulated pigment clumps. These can be observed through the retinal layers to various extents. It would appear that the distance through which the pigment clumps travel is directly related to the energy density of the exposure beam. Some of the pigment clumps come to rest within the retinal layers themselves; others might be dislocated in the preretinal space, and more intense ones may travel for considerable distances through the vitreous body, leaving channels through which choroidal hemorrhage follows. In the immediate surrounding of these retinal channels, multiple diffracting globules are frequently seen which stain positive with fat - 0 - red for free lipoids.

In very large areas of exposed retina, as described by Jones and McCartney [5], the border of the lesion is not as sharply demarcated as seen in smaller burns. Such lesions as produced in Maxwellian view in the intact monkey eye and at low energy densities on the retina are frequently not visible by ophthalmoscopy. However, under histological examination, damage could always be demonstrated and consisted primarily of retinal detachment, pigment loss from the retinal pigment epithelium, choroidal damage, micro-lesions with scattered pigment granules, degeneration of the inner and outer segments of the receptor cell layers, pyknotic nuclei, and free blood cells.

Histochemical Findings.

It has been stressed [2] that ophthalmoscopic visible minimal lesions and histological minimal lesions certainly do not represent even an approximation of true visual functional lesions. Therefore, other avenues have been explored in order to approach the actual "threshold" level for retinal damage. It was assumed that enzyme inactivation should represent a more critical and sensitive method of determining damage, either transient or permanent, to the retina than obtainable with ordinary histological staining techniques. The two systems studied were succinic dehydrogenase and DPNH diaphorase. Since the study was performed in rabbit eyes, (because of the similarily to the human eye in the respects as outlined previously), DPNH diaphorase was finally selected as the more sensitive indicator of damage in spite of the fact that it has been argued that there is no "real" enzyme in the retina of that description. Succinic dehydrogenase intensively stains within the ellipsoids of the receptor cell layer, presumably identifying mitochondria; however, this is the only location within the neural retina where staining can be observed histochemically. On the other hand, DPNH diaphorase activity, as evidenced by its staining reaction, can be demonstrated in the ellipsoids of the receptor cell layer as well as Muellers fibers and also in the ganglion cell layer of the retina of the rabbit eye [31,33].

This fact is of value in studying the extent of the destruction after laser or light coagulation to layers of the retina other than the retinal pigment epithelium and receptor cell layers.

One phenomenon found in this study should be briefly mentioned. The borderline pattern of lesions produced at long exposure times showed a sloping margin of inactivation of enzyme activity whereas the borderline between exposed and nonexposed retina at short exposure times (microsecond ranges) showed a very sharp delineation of enzyme inaction. This phenomenon may have been caused by the different thermal gradient in the periphery of the lesions, though this can only be explained with difficulties on a theoretical basis [34].

A previously mentioned study [2] has made it evident that histochemical methods are important in studying various enzyme systems and should be included in future investigation to determine lower threshold data for vital physiological systems, though one should be aware of the fact that different enzyme systems react quite differently to thermal and other insults.

More critical data may be obtained if histochemical methods are combined with electron microscopic techniques to study enzyme activity in the pigment epithelial cells themselves. With "routine" histochemical methods in normal cryostat sections, possible mitochondrial staining is obscured by the melanin granules; however, with refined Nitro-tetrozolium staining for electron microscopic sections, this difficulty can be overcome.

Electron-microscopy.

An electron microscopic comparison of retinal lesions produced by white light and laser radiation at equal exposure times was conducted to study the details of morphological changes at a cellular level [35-37]. This comparison has shown that for both types of irradiation the apparent site of the earliest tissue changes seem to lie within the pigment epithelial cells. Though the examined lesions were slightly above threshold, examination of peripheral zones of such lesions reveal, to some degree, threshold cellular damage on a morphological basis. Within these marginal cells the fragile system of smooth-surfaced endoplasmic reticulum occupying the apical and midzonal cytoplasm was grouped into two major features: 1) patchy and focal densification of the adjacent ground substance to membranes and 2) focal densification of membranes. This granulation effect was particularly prominent in the lamellated receptor outer segments. However, a similar granular effect was also seen in the pigmented epithelial villi, in the mitochondria, and within the photoreceptor synaptic expansions. Since within the latter structure the normal synaptic densities become exaggerated with densification of the limiting plasma membranes, whereas such changes were not observed in the apposed plasma membranes of either the second order of neurons or the adjacent glial cells, it has been considered as evidence for lack of transsynaptic degeneration within the time interval of the experimental observation (5 hrs. post irradiation). There was no specific difference in the intercellular degeneration in lesions produced by light coagulation or laser exposures. The boundary between exposed and nonexposed retinal pigment epithelium was rather sharply demarcated, showing granulation effect of the photoreceptor outer segments, vacuolization of the endoplasmic reticulum, and disturbances of the infolding of the basal membrane of the pigment epithelium of the exposed cells, while the immediate neighboring cells did not show any pathological changes. In general, the observations support the hypothesis that the intercellular changes are non-specific to this particular insult. Similar morphological changes can be produced with various forms of trauma. It is of interest that minimal lesions examined by this technique required retinal energies (density and irradiance) identical to those visible with histological techniques. As mentioned under "Histochemistry", refined techniques, utilizing histochemical techniques in combination with electron microscopy in order to demonstrate enzyme activity within the mitochondria of the retinal pigment epithelial cells, may lead to observations and demonstration of damage to enzymes systems below energy levels which produce the morphological changes as described in this paragraph.

Other Examination Methods.

Chan _et al._[4] has shown by agar-tissue electrophoresis that alterations of soluble retinal protein occur after light coagulation. In this particular study it was found that certain alterations were greater if long exposure times had been used (500 ms) in comparison with short exposures (175 μs). The exposure energy used in that study was 40% above the energy level for producing minimal visible ophthalmoscopic lesions. The image diameter of the exposure beam on the retina was 1 mm in diameter. The alteration of soluble retinal protein due to the coagulation effect was demonstrable not only within the area of irradiation but also outside the lesion in the adjacent retina, more than 2 mm from the center of the lesion.

McNeer _et al._[3] showed by rather gross electroretinographic techniques that a significant reduction of the b-wave could be observed at energy levels 50% below that which produced ophthalmoscopic minimal visible lesions. The disadvantage in this particular experiment was the necessity of multiple exposures in the posterior pole of the eye in order to demonstrate this electroretinographic finding. Although the observation of the reduction in the b-wave was reproducible, it is not possible to conclude a loss of visual function. However, more refined techniques utilizing the retinal response to stimulation after light exposure may provide valuable information. The temporary interference with ERG recordings after laser exposure reported by Allwood and Nicholson[38] is certainly of interest and raises the question of interferences by vibrational disruption of physiologic transport.

High speed cinephotography during actual laser exposure in order to study effects other than thermal had been emphasized by the reviewer [39] using STL image converter camera which allows sequence photography at retinal exposure itself and in addition precise timing of those events in vivo and in vitro systems. Any other high speed cinematography is limited by the relatively slow recording. Zaret et al. [28] nevertheless showed valuable data with normal high speed cinematography documenting pressure waves in biological systems upon exposure, a phenomenon described before by Amar et al. [40]. Also the method of fluorescein cinematography recently advertised by various investigators for studying retinal damage after laser or light exposure was first suggested by Zaret et al. [28] and this technique has added another interesting examination and evaluation technique to the existing armamentarium in evaluating retinal injury.

REVIEW AND DISCUSSION OF EXPERIMENTAL WORK

In this chapter, only articles dealing with accurately measured physical parameters in the production of minimal retinal lesions are reviewed. Because of the great variety of physical parameters, differences in applied units of measurement and constantly new published values, this most important facet of laser evaluation is at the same time the most vulnerable, most changing, most critical, and most controversial one.

The production of mild ophthalmoscopic visible retinal lesions in the rabbit retina by white light of the Xenon high pressure arc, pulsed ruby laser and q-switched ruby laser as a function of average irradiance and exposure time has been studied by various investigators [1-7,28-30,34-37,41-62]. Work conducted by Ham, Geeraets, Guerry and co-workers [41-46] ranged in exposure times from three minutes with the Xenon high pressure arc down to 28.5 ns for the q-switched ruby laser with an overlap of white light and pulsed laser radiation in the microsecond range (200 μsec). The image sizes of the exposure beams on the retina were equal for all three sources of irradiation and measured from 100 μ to 1 mm in diameter.

White light exposures longer than 4.0 ms were obtained by operating the Xenon lamp continuously (CW) with a KG-3 filter introduced in the beam to remove wavelengths greater than 950 mμ. For exposure times between 175 μs and 4 ms, the white light source was electronically pulsed, which resulted in a shift of the emission spectrum almost entirely into the visible range [32]. It was found that for longer exposure times, say longer than approximately 10 ms, the lesion size depended markedly on the exposure time. The lesion size appeared to be smaller than the image size for low doses of thermal energy, while for large doses of energy, the lesion exceeded in size the image size of the exposure beam on the retina.

For short exposure times, in microsecond ranges, the image size and size of the lesion (minimal lesion) were approximately equal. This holds true for laser exposures as well as white light exposures. The required irradiance for producing mild lesions with the pulsed ruby laser source (200 to 300 μs) and the pulsed Xenon lamp (175 μs) measured approximately

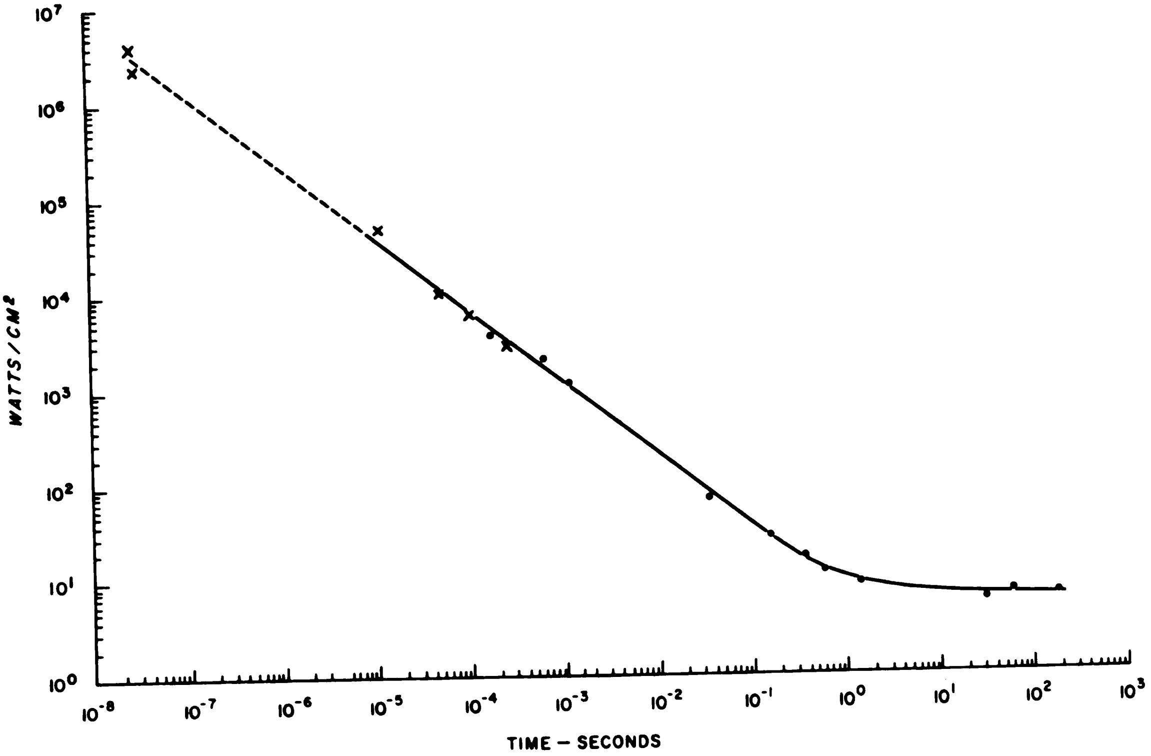

Figure 4. Log-log plot of average irradiance in watts/cm^2 vs exposure time in seconds for mild lesions in the rabbit retina. Image diameter on the retina 800 μ.

● data for white light $<$ 950 nm.
x data for ruby laser, 694.3 nm.

(Ham et al., Trans. N. Y. Acad. Sci. 28:520, 1966)

3-4 KW/cm^2 for an image size of 800 μ diameter on the retina.

For q-switched ruby laser irradiation (30 ns) the average irradiance measured 2-5 MW/cm^2 for the production of mild lesions. The ophthalmoscopic and histological appearance of those lesions in comparison with those produced with the normal pulsed ruby laser and the Xenon light source were different as described in the previous chapter on the histology. The region between 175 μs and 30 ns exposure times needs to be investigated. Figure 4 shows graphically the average irradiance in watt/cm as a function of exposure time in seconds for mild lesions in the rabbit retina. The image size on the retina for the computation of this plot was 800 μ. From this figure it becomes obvious that for long exposure times the curve tends to become parallel to the abscissa, thus defining for a given image size a limiting retinal irradiance for mild lesions. This means that at some temperature above ambiant and for relatively long periods of time, the retinal tissue apparently is not undergoing any ophthalmoscopically visible alteration.

Though it has been demonstrated in experiments by Ham <u>et al</u>.[1] that at long exposure times the required energy apparently decreases with the increase of image size of the lesion, studies performed by Jacobson are not in accordance with this observation. Jacobson and co-workers[47] grey chinchilla rabbits for their retinal burn threshold data. The range of retinal image sizes in their experiment varied from 0.65 to 4.4 mm in diameter and the exposure times ranged from 25 to 150 ms. The instrument used was a Xenon high pressure lamp in the Zeiss light coagulator, with provisions for short exposure times. The lesions were produced and characterized as a function of time of exposure, irradiance, image size, and spectral characteristics of the incident energy. Lesions in the ocular fundus were clinically subdivided into seven subgroups of intensity: a score of 1 meant no lesion was observed after five minutes and 3 + was the heaviest lesion, with explosion of the retina. A so-called "E-burn" was chosen by the investigators to represent the threshold lesion for several reasons: 1) the minimun lesion is one that the observer could discover with indirect ophthalmoscopy with some degree of consistancy; 2) damage produced was irreversible as proven by a pathological study of the lesion and 3) there was no evidence at the time of injury of any coagulation of the involved tissue. The authors further remarked that they did not consider the "E-burn" as an absolutely minimal insult. In their discussion the investigators come to the conclusion that for a given irradiance the threshold dose increases with increase of the retinal image size. This conclusion is in contradiction to the findings reported by Ham, Geeraets <u>et al</u>.[1,44]. One must not forget that the image sizes with which the <u>two</u> groups of investigators have experimented are different, and therefore extrapolation of Jacobson's data down to the image sizes of the experimentation by Ham, Geeraets <u>et al</u>. is probably not justified. This becomes even more evident since in regions where the image sizes of the exposure beams on the retina were the same in both investigations (about 1 mm in diameter), the data of Jacobson and Ham <u>et al</u>.(1) are in agreement at approximately 1-2 cal/cm^2.

Furthermore Jacobson and co-workers stated that a higher energy dose was necessary to produce a lesion when the near infrared was included in the spectrum of the irradiating beam as compared with exposures to light within the visible range only. This is in agreement with data reported by Ham, Geeraets et al. and in accordance with experimental results by Bredemeyer et al.[61].

Irradiation of large areas of the retina were also reported by Jones and McCartney[5]. These investigators, however, used the normal pulsed ruby laser instead of a white light source. The pulsed ruby laser radiation in their experiment was presented in Maxwellian view to the intact monkey eye. The pulse duration was about 2.0 ms, and the flash energy was varied between 1 and 250 j. The investigators stated that energy levels above 100 j produced a marked degree of periorbital edema. But even below these high energy levels the gross findings showed corneal pitting, hemorrhages into vitreous with bubble formation, and loss of light reflex. Histologically the authors observed extensive damage in the pigment epithelium and choroid associated with secondary retinal detachment and degeneration which extended peripherally to the area which had been exposed. These investigators state that at a large retinal subtense moderately severe lesions show significantly different clinical appearance as compared to those of small retinal image size, the lesions were frequently not visible by ophthalmoscopy whereas the lesion could be demonstrated by histological techniques.

The authors used Macaca cynomolgus and cercocedus torquatus atys. The retinal area exposed under Maxwellian view measured about 78.5 sq mm or 24% of the total retinal area. The eyes were enucleated at different time intervals, up to fifteen months after exposure. Histological sections were stained with hemotoxylin and eosin, gallocyanin or Mallor's azan aniline blue. Four Macaca cynomolgus received single pulsed laser exposures in both eyes; the retinal subtense of these exposures was 43.2 degree which gave a retinal area of 1.13 cm^2. The energy per flash ranged from 1.2 to 7 j, delivered in 1.5 ms, and the energy density ranged from 1.0 to 6.2 j/cm^2. These animals were sacrificed six days after exposure.

According to the authors' outline and tables 1 and 2 (see ref. 5) the lowest exposure energy was 5.0 j and an energy density of 1.53 cal/cm^2 and the examinations were carried out one and six days after exposures. These exposures were performed on Macaca cynomolgus.

In a second series of exposures on four Macaca cynomolgus, the energy density ranged from 1.0 to 6.2 j/cm^2 with a calculated image diameter of 11.25 mm. The authors stated that at close examination and energy densities below 2.6 j/cm^2 delivered in 1.5 ms no clinically observable lesions could be seen. However, six days after exposure they observed in three eyes some cobblestoning and small irregularites of the fundus. They also described a grayish appearance of the fundus immediately after exposures and a loss of definition of small surface vessels six days after exposure. At energy levels between 3 and 6 j/cm^2 they observed immediate elevation of the retina and loss of light reflex. In these cases the retina became completely detached within six days after exposure.

The authors postulate that the primary damage after exposure to the pulsed ruby laser occurs in the retinal pigment epithelium, caused by localized temperature elevation with involvement of the outer segments of the receptor cells. The primary injury then creates secondary degenerative changes involving the receptor cell layer with degeneration, loosing of the outer segment-pigment epithelial junction, fluid infiltration, and finally complete retinal detachment. This assumption can well be compared with the electron microscopic findings as described by Fine and Geeraets [35] which presented similar observations at the primary site of injury in the retinal pigment epithelium and outer segments of the receptor cell layer with secondary degeneration of the first neuron.

If one takes the lower value of energy levels quoted by Jones and McCartney [5] 1.0 to 6.2 j/cm^2 for image diameter of 11.25 mm) in conjunction with their statement that for all energy levels histological damage could be demonstrated, one finds that their minimal dose for this particular exposure time and large irradiated areas are in fair agreement with the minimal dose for production of lesions of relatively small image diameter i.e. 1.0 j/cm^2 vs. 0.8 j/cm^2, respectively reported by Ham *et al.* [44].

The exposed areas of the retina were almost equal in the experiments of Jacobson *et al.* [47] and Jones and McCartney [5], but the exposure times were different, 2 ms as opposed to 25-150 ms. The extrapolation of the data is, therefore, of doubtful value.

The threshold values for lesions produced with a normal pulsed laser and with the q-switched laser of Bergqvist, Kelman and Tengroth [48,54] are in fair agreement with data of Ham and Geeraets, who used equal image sizes. For lesions smaller than 100 μ in diameter, - in Bergqvist's 50 μ, - the power density for q-switched lesions required 400 MW/cm^2. This is an increase of approximately 1000 times above the threshold for normal pulsed laser lesions in their study. The possibility of the introduction of artifacts pertaining to such high energy levels is discussed in a following section.

Zaret, Ripps, Siegel and Breinin (1963) [49] gave as an appropriate threshold dose for lesions (produced with a pulsed ruby laser of 2.5 ms duration and an image diameter of 150 μ), a value between 6.45 and 0.65 cal/sq cm. However, since the image diameter was only an estimate, these results have to be taken with caution, as the authors implied.

In a more recent report Zaret and co-workers [50] used the Douroucouli monkey eye for their investigation of minimal retinal lesions produced with q-switched laser action. The laser used was a TRG model 104 q-switched laser action. The laser used was a TRG model 104 q-switched ruby laser. The output of the laser was 0.3 j with a peak power of 10 MW. The image sizes on the retina were experimentally verified by implanting stainless steel microspheres of 0.025 inches in diameter into the vitreous and measuring these microspheres photographically after they had been attached to the retina by retrobulbar magnets. The magnification factor by photographic recordings was 3.15. The authors calculated from these measurements that the focal length of this monkey eye was 18.3 mm. The retinal image sizes measured 0.47 mm, 0.67 mm and 1.86 mm. They described the ophthalmoscopic findings of minimal lesions as an initial darkening or graying of the exposed retinal area which sometimes seemed to be transient. Two annular zones could usually be distinguished for minimal lesions which surrounded the exposed portion. In moderate lesions choroidal hemorrhage occurred that extended within the plane of the choroid and in deep retinal layers. A further increase in intensity resulted in hemorrhages which were confined to the area of chorio-retinal junction. With still higher energy density, profuse hemorrhaging occurred extending through the retinal layers and frequently into the vitreous.

The energy density range for the production of minimal lesions to the more severe ones extended from 0.06 to 1.8 j/cm^2.

The findings described by the authors, that different area size of illumination did not noticeably influence their threshold for injury, agree with the observations of Geeraets and Ham at that exposure time. However, their observations that heavily pigmented fundi, although generally requiring lower threshold energy for the production of minimal lesions than that for normal pigmented fundi, were not statistically significant, does not correspond with observations made by Ham and Geeraets, nor are they in agreement with measurements made in vitro examination on pigmented cells exposed to q-switched laser [63,64].

Interesting observations were made by Zaret et al. [50] using high speed cinephotography. During the exposure of the retina with the unfocused beam intensity of 10 MW/cm^2 they observed two phenomena: 1) production of a mechanical force and 2) indirect evidence of the production of aplasma within the eye. These observations support reported findings by Geeraets(39) on the production of a plasma under q-switched exposure of the retinal pigment epithelium in which the exposure time measured 30 nsec, whereas the duration of the plasma lasted for several microseconds and the duration for the produced shock-wave lasted about 5 ms.

Vassiliadis and co-workers [29] reported observations on exposures of rabbit retinas to normal pulsed ruby laser exposures. Examination was carried out 24 hrs. after exposure. In the section on long pulsed ruby laser exposures, the authors do not give any image sizes of their exposure beam on the rabbit retina; however, it may be assumed from their q-switched ruby laser exposures that the image sizes on the retina are equal (100 to 150 μ diameter). In this report, the authors recommend histochemical methods for determination of retinal threshold lesion which supports similar recommendations made previously [2]. They added other techniques to those used previously and mentioned in this report under "Histological Findings".

Energy levels for the production of minimal visible retinal lesions produced with normal pulsed ruby laser are not contained in the report by these investigators since exposure times, exact image size, and exact energy were not clearly defined. Taking, however, their threshold energy dose for q-switched ruby laser radiation, which is in agreement with Ham et al. and other experiments discussed in this paper, the quoted threshold dose for normal pulsed ruby laser and the human eye by one of the co-authors (Zweng)[42] was quoted as 20 j/cm^2. This value appears extremely high and needs verification.

Beside their work with effects of normal pulsed laser action on rabbit eyes, the authors have conducted studies with q-switched ruby laser on the rabbit retina and the Rhesus monkey. The authors defined clinical visible threshold lesion as just barely visible changes by ophthalmoscopy within 45 to 60 minutes after exposure. They state that the only method of investigating the sub-visible lesions that produce irreversible damage would be by histochemical techniques. Their stated retinal dose for the production of minimal lesions produced by q-switched laser action (8 nsec), and "assumed retinal spot size of 100 to 150 μ" was given as 0.05 to 0.1 j/cm^2 for a 50% probability of the development of the lesion. This energy level is in agreement with the above mentioned values quoted by various investigators for this retinal image size.

The authors feel that the threshold for histological visible lesions would be lower than the quoted threshold for ophthalmoscopic visible lesions although they do not demonstrate histological proof for this assumption. In investigations carried out by Geeraets et al. it has been shown that the threshold level for histological and even electron-microscopic examination techniques was essentially the same as that for ophthalmoscopic visible lesions, providing special ophthalmoscopic techniques were used. The only techniques by which lesions could be identified below the clinically visible threshold were histochemical staining techniques for enzyme inactivation and electrophoretic examination for possible demonstration of protein alterations of the retina [2,3].

Other observations by these authors, particularly with regard to histological description of the differences in the appearance of lesions produced with normal pulsed ruby laser and those produced with q-switched lasers, correspond generally to the descriptions given by other investigators during the last several years and are discussed in this report.

In more recent studies using long-pulse ruby laser, q-switched ruby laser, and a mode-locked ruby laser Vassiliadis et al. [65] and Zweng et al. [66] presented data for minimum spot sizes on the retina of Rhesus monkey. The data were obtained for exposure of the paramacular region. Macular threshold lesions were produced with long-pulse laser exposures. The authors stated that the threshold for macular lesions indicated that this location is 2.2 times more sensitive to laser-induced injury than the paramacular region. Threshold criteria were based on ophthalmoscopic visible lesions one hour after laser irradiation. About 1.1 mj was given for a 50% probability of retinal damage in the paramacular region for long-pulse ruby laser irradiation, corresponding to an energy density of 56 j/cm^2. For the macular region approximately 0.5 mj (2.6 j/cm^2) were required for similar conditions and criteria. Spot sizes were given as 40 to 60 μ and pulse duration with about 1.7 ms. It should, however, be stated that the lesions illustrated in this report appear to be well above the general criteria adapted for ophthalmoscopic visible minimal lesions.

Data given for minimal lesions produced by q-switched laser irradiation in the rabbit eye were given with 8 μj for a 50% probability and for 8 ns exposure time and about 100 μ retinal diameter. This corresponds to about 0.1 j/cm^2 retinal energy density. In the Rhesus monkey eye spot sizes of approximately 25 μ were estimated although for the most part they averaged about 50 μ in diameter. The retinal energy density for these spot sizes was calculated with 0.8 j/cm^2 or peak power density of about 100 MW/cm^2 for clinically visible minimal lesion. For histological detection of retinal injury about half of this energy density was sufficient according to these investigators.

In a more recent paper by Kohitiao and co-workers [7], who used normal pulsed laser and q-switched laser for production of minimal retinal lesions in gray chinchilla rabbits, the quoted energy levels for the production of minimal retinal lesions for both modes of laser action were quite different from any of the previously published reports. For the normal pulsed laser an exposure time of 500 μs was implied. The retinal image size of the exposure beam measured 250 μ in diameter. Their criteria for a minimal threshold lesion was based on a LF 50 (lesion factor of 50%). The authors accepted as threshold lesions those which appeared 24 to 48 hours after exposure. Their retinal dose for minimal lesions produced by the normal pulsed ruby laser was given as 0.16 i/cm^2, which is about 5 times lower than the threshold given by other investigators.

The same investigators gave a threshold dose for lesions produced with q-switched pulses of 80 ns duration and equal image size of 250 μ on the retina as .0045 j/cm^2. The latter value is about 16 times lower than the ones reported by Ham, Geeraets <u>et al</u>., and other investigators. In other words, between the threshold level for production of minimal lesions with normal pulsed ruby laser action and q-switch action, their data show a factor of 40, whereas the same factor in Ham's experimentation is only 10.

Ruby vs. Neodymium Laser

Little has been reported in the literature on retinal lesions produced by neodymium laser either in the pulsed or the q-switched mode [51,67]. In particular no exact energy levels for the production of such lesions has been presented. In the following, a comparison of lesions produced with the ruby laser and neodymium laser is made.

At the wavelength of the ruby laser (694.3 nm) the ocular media absorb approximately 6% of energy incident on the cornea; for the neodymium wavelength (1060.0 nm), approximately 50% of the energy incident on the cornea [24-26] is absorbed. The loss of energy by absorption, scattering, and reflection in the darkest human retinal pigment epithelium (PE), amounts to about 40% for ruby laser wavelength rather than the 15% of neodymium [25] in the human eye. Reflection from the pigment epithelium and choroid is approximately 3 to 5 times greater for the neodymium wavelength than for the ruby wavelength(26) in the human eye. The data for loss of energy at these two wavelengths within the darkest pigmented human choroid are approximately 56% (694.3 nm) and 23% (1060 nm) [25] for ruby and neodymium respectively.

It should be pointed out that for short pulse durations, such as those present in normal pulsed ruby or neodymium laser (µs to a few ms), and low energy levels which produce only minimal ophthalmoscopic and/or histological lesions in the retina, only the retinal pigment epithelium and its immediate neighboring structures are involved. The reason for this has been discussed previously [1,2,44,68]. For longer exposure times, that is greater than 10 ms, and for moderate to heavy lesions produced with higher energy levels, absorption within the choroid contributes increasingly to the extent of the lesion produced. At very high energy levels, even with short pulses, the absorption of neodymium wavelength (1060 nm) within the ocular media certainly makes for an additional complicating factor, though one may state that with a single, heavy accidental exposure severe chorioretinal disruption can occur, thus causing injury to the ocular media to be relatively insignificant. However, the greater absorption of the neodymium wavelength in the OM makes this wavelength less desirable where relatively frequent and repetitious exposures (1 sec intervals) are required with energy levels resulting in mild to medium chorioretinal reactions, that is, in the range of clinical therapeutic use.

Although the absorption for 1060 nm in the OM is considerably greater (50%) than that for the ruby wavelength (6%) and lower in PE (15% as opposed to 40%), one cannot conclude that for those two wavelengths the primary site of injury is at different topographic locations within the retina. The PE measures about 10 µ in thickness, while that of OM for the human eye can be given at a minimum of approximately 22000 µ. The neural retina measures about 500 µ in thickness posteriorly and about 250 µ at the center of the fovea. These considerable differences in "thickness" of the absorbing structures make it evident that the energy lost by the various means of energy dissipation per unit thickness is still considerably greater in the PE as compared to the neural retina. This becomes evident in comparing the histomorphological changes which occur in the retinal pigment epithelium and in the adjacent retinal and choroidal structures after exposure to the ruby and neodymium laser wavelength.

Preliminary data for energy densities and power densities of neodymium laser radiation were obtained in chinchilla and dutch rabbit eyes. With exposure times of 200 µs and image size of the exposure beam of approximately 800 µ in diameter on the retinal pigment epithelium, the energy density for an RD 50 lesion (lesion produced in 50% for exposures at this energy level) was about 5 to 6 times higher for the neodymium wavelength than that of the ruby laser wavelength. The same observation was made using both lasers in the q-switched mode (30 ns exposure time). This factor of roughly 5 to 6 in required energy density for the neodymium wavelength for production of minimal retinal injury can in part be explained by the greater reflection from and lesser absorption within the retinal pigment epithelium [26].

In the past, rabbits and monkeys have been the experimental animals of choice in determining levels of retinal damage after exposure to radiation sources like the sun, nuclear fireballs, xenon lamps, and lasers. The demand for a realistic evaluation of the retinal burn hazard from nuclear weapons and the growing hazard from laser sources accentuate the need for an accurate extrapolation of animal data to humans. The clinical technique of light coagulation of the retina has provided some information which can be correlated with animal data but generally speaking such data are difficult to use because they are obtained under pathological conditions and do not involve exposure of the fovea.

Foveal exposure in a human volunteer, a 51 year old white male, has been performed recently [69]. The eye had to be enucleated for a choroidal melanoma. A complete ocular examination revealed clear ocular media, visual acuity of 20/20-1 (corrected) and normal foveal reflex. A choroidal melanoma was located in the upper nasal quadrant with intra - and preretinal hemorrhages present. There was no central visual field defect (1 and 3 mm white test targets). Photopic and scotopic adaptation times (Goldman-Weeks Adaptometer technique) were within normal limits.

The focal length, as determined by ultrasonogram, was calculated to be 17.5 mm. Retinal light exposure was than performed, using the "research light coagulator" described in a previous paper(70), which utilizes a Xenon high pressure lamp as the light source and a KG-3 filter introduced in the optical pathway. This filter restricts the radiation spectrum to the visible region, eliminating wavelengths beyond 950 nm. The angle of divergence of the light beam entering the eye was 4.5°. The calculated image diameter of the beam on the retina, based on a focal length of 16.5 mm for the 2 dpt. myopia of this patient was 1.37 mm in diameter. The exposure times ranged between 130-140 ms, and each exposure was monitored and recorded separately.

The first exposure was made in the midperiphery in the 11 o'clock meridian. The calculated retinal dose for this exposure was 7.9 j/cm^2 No ophthalmoscopic visible lesion developed within the next 18 hours.

Another exposure was made in the 10 o'clock meridian, increasing the retinal dose to 9.2 j/cm^2. This exposure caused a very mild change in the retina within about 5 minutes after exposure and seen with the ophthalmoscope using red free light. Another exposure using 9.6 j/cm^2 as the calculated retinal dose was made in the 9 o'clock meridian and produced results comparable to the 9.2 j/cm^2 exposure. Accordingly, 9.6 j/cm^2 was accepted as a valid estimate of threshold dose according to the criteria used in this experiment.

A diaphragm was then inserted in the light beam, reducing the energy output by 50% but leaving all other experimental parameters unchanged. The macula was exposed to this retinal dose (4.8 j/cm^2). Immediately after exposure, visual acuity, visual field and adaptometry were repeated under the same conditions as carried out prior to the exposure.

Corrected visual acuity was 20/25 + 3; the visual field was unchanged, and there was a slight delay in cone and rod adaptation times. However, all tests showed pre-experimental data within 2 hours and 30 minutes after exposure.

Another exposure was then performed. This time it was decided to irradiate the macula with a retinal dose equal to that required to produce a minimal visible lesion in the midperiphery. The first exposure in the midperiphery was made with a retinal dose of 10 j/cm^2. No visible lesion developed over the next 15 minutes and did not appear over another 15 hours of observation. Accordingly, a second exposure to a calculated retinal dose of 12.2 j/cm^2 was given to the midperiphery. A very mild lesion developed within three to four minutes after exposure. The macula was then exposed to a calculated dose of 13.0 j/cm^2. No ophthalmoscopically visible lesion could be detected over the next 15 hours. There was loss of the foveal reflex which was still present the following morning when the patient received his last examination.

Immediately after this exposure, visual acuity, visual field, and adaptometry tests were performed again. The visual acuity corrected was similar to the previous experiment, 20/25 + 3 corrected. There was no scotoma, but the patient reported an after image which was "about the size of a goose egg" at 1 meter distance from the screen. Viewing a black background the center of the image was "greenish, surrounded by a bluish ring". Viewing a white background the after image was purple. This after image faded slowly but was still noted by the patient 5 hours after the exposures. The adaptometry curve for cone and rod adaptation was almost identical to the one obtained after the first experimental light exposure. There was again a slight delay in cone adaptation and rod adaptation beginning about 10 minutes after the completion of light adaptation. Original values were approached after approximately 30 minutes, at which time the test was discontinued because of the increasing tension of the patient.

Fourteen hours after last macular exposure the visual acuity was 20/20-2 corrected and no visual field loss could be detected with various size of white or colored test objects. There was no after image observable by the patient (9 hours after the last exposure) and the adaptometric values had returned to pre-exposure levels.

Steady State Laser Hazard

With the increase of power output from CW or steady state operation of gas lasers and semi-conductor diodes, special precaution has to be taken to prevent retinal damage. Injury may derive from prolonged single exposures or accumulated exposures with the possibility of late sequellae. The latter are at present only mentioned as theoretical possibility since no well controlled experimental results have been made available to substantiate this assumption. However, the data reported by Noell[57], Dowling [60], Kuwabara and Gorn [58,59] certainly call for meticulous investigation of such potential photodynamic retinal injury.

Under normal conditions the output beam from these laser sources are extremely parallel, and hence the image size of the beam on the retina is diffraction limited if no optical systems are used in the pathway of the exposure beam.

Jones and Montan [71] have described ocular hazard for exposure to CW laser such as the He-Ne gas device. These authors calculated that 10^{-6} watts could be regarded as a safe power level on the retina even if the energy is confined to a 10 μ image diameter on the retina. Though this image size may be an underestimate [72], it provides a factor of safety in so far as the energy density is concerned. This safety factor, however, is opposed by the factor of energy dissipation by conduction from the irradiated image to the surrounding unirradiated tissue in proportion to the temperature gradient. For long exposure times it has been shown [1] that the energy required for producing irreversible retinal injury decreases with the image size of the exposure beam on the retina.

DISCUSSION AND CONCLUSIONS

The reported data on energy density incident on the retina for the production of ophthalmoscopically visible, minimal lesions, utilizing white light, are in fair agreement among several independent research groups if exposure times and retinal spot sizes are taken into account. Apparent discrepancies between data reported by Jacobson et al. [47] and those obtained by Ham et al. [43] may not be true disagreements since exposure techniques and image sizes were quite different in the two studies.

For lesions produced with pulsed ruby lasers, the reported data are again in agreement if the physical parameters relating to the production of these lesions are equal. For image sizes ranging from 100 μ to 1.0 mm diameter on the retina and exposure times ranging from 200 μs to approximately 2 ms, the retinal dose (j/cm^2) range from 0.7 to 1.0 j/cm^2). This value is in agreement with Jones and McCartney [5] up to lesions as large as 4.4 mm in diameter, although these investigators had quoted their visible threshold prior to this last report with 0.01 j/cm^2 for q-switched ruby laser exposures and large image sizes in the monkey eye [52]. The only large scale deviation known to the author has been reported by Kohtiao and co-workers [7] who give retinal energy densities of 0.16 j/cm^2 for image diameters of 250 μ and exposure times of 500 μs. Their values are lower by a factor of 5 from the data obtained by others [44,48].

Discrepancies occur if the image size on the retina is reduced below 100 μ diameter. However, with the in vivo examination techniques employed, it becomes increasingly more difficult to recognize very small lesions by ophthalmoscopy because of the lack of contrast between very mild lesions and the surrounding normal retina. This in turn requires higher energies to obtain more severe lesions so that they may be recognized. Moreover, it is doubtful whether the rabbit eye, because of its poor optical quality, can resolve images smaller than 100 μ.

Similar observations hold for q-switched ruby laser lesions. For exposure times ranging from 5 to 50 ns, the retinal irradiances required for the production of minimal visible lesions range between 2 and 5 MW/cm^2 for image diameters from 100 μ to 1 mm. The threshold value for an RD 50 lesion reported by Ham et al.[45] and Geeraets et al.[41] is 0.07 j/cm^2 or 2.3 MW/cm^2 at an exposure time of 28.5 ns. The only large scale discrepancy from this value as of now is that reported by Kohtiao and co-workers[7]. While their value for multiple-spiked ruby pulse was 5 times lower than ours, their lesion, which was produced with a q-switched ruby laser 250 μ in diameter and 80 ns exposure time, was .0045 j/cm^2, a value 16 times lower than that reported by us and other, a discrepancy discussed in this paper. However, there are many possible explanations for this discrepancy when one considers the method used by these authors to produce lesions.

When the image diameter is reduced below 100 μ it would appear that the retinal dose for production of minimal retinal lesions is significantly greater than that for larger image diameters[1]. Bergqvist, Kelman and Tengroth[48] reported power densities of 400 MW/cm^2 when the image size was reduced to 50 μ in diameter. However, in more recent communications[53] these investigators indicated that artifacts caused by previously mentioned difficulties in recognizing minimal lesions of very small diameters may well have contributed to high dosage levels. Moreover, there is no real agreement among authorities as to the limiting size of retinal spots for the human, monkey, or rabbit eye. This in itself may introduce another source of error if irradiances are calculated on the basis of estimated spot sizes of the exposure beam on the retina. In recently published data by these investigators[54], the required power density for q-switched ruby laser lesions of the retina were even of a wider range depending on "calculated" image sizes on the retina. In this report the power density for an 8 μ in diameter lesion in the rabbit eye was given with 36000 MW/cm^2. Realizing that an image size of a diameter that small is almost impossible to achieve in the rabbit eye with its relatively poor optical qualities, these published data certainly call for a very detailed, exhaustive and final clarification of the question of the influence of image size and energy levels. An in vitro attempt to clarify these discrepancies has been made[73].

While the thermal concept of retinal injury most likely holds for exposure times in microsecond ranges Vos[74,75], Ridgeway[76], Ham and co-workers[44] Geeraets and Ridgeway[68], Hayes and Wolbarsht[77], Makous and Gould[56], Wray[78] and Spells[62], this concept is inadequate to explain all biological effects occuring in retina and choroid, particularly at high power densities (MW/cm^2) and short exposure times (nanoseconds) as produced by q-switched laser exposures. During these extremely short exposure times heat conduction does not extend beyond 0.1 μ from the site of absorption. Taking an average diameter for a retinal pigment epithelial cell as being approximately 10 μ and a melain granule size of from 1 to 3 μ, the incident energy from a giant pulse of laser light would in the early stages of the pulse be absorbed by the anterior portions of the pigment granules with a resulting high temperature rise in these structures. This in turn may lead to ionization and possible formation of a plasma which would be opaque to additional incoming photon. Shock waves and acoustic signals, Raman and Brillouin scattering, frequency doubling and other non-linear phenomena may produce biological effects in addition to thermal effects and before heat conduction would play a significant role. It seems that these biological effects of q-switched lasers are relatively independent of image size on the retina. Some support for this viewpoint comes from in vitro observations on cellular death for chick retinal epithelial cells in tissue culture when exposed to a q-switched ruby laser beam at 30 ns [73]. The LD 50 dose (50% change of cellular death from this energy density) was identical for an approximate spot size of 20 μ and 135 μ diameter at the cellular plane. This energy dose was 1.2 j/cm^2, or an irradiance of 3.4 MW/cm^2, which is in agreement with the in vivo observations for retinal image diameters greater than 100 μ [44]. Observations in support of this but using normal pulsed ruby laser radiation have been made by Feick and co-workers [79].

It should be stressed that retinal injury may occur from photochemical processes as described most recently by Noell [57], Dowling [60], Gorn and Kuwabara [58,59], Rounds *et al*. [75].

Data obtained from the one human volunteer should be evaluated separately. The calculated retinal energy densities required to produce minimal lesions in the periphery of this human fundus were significantly higher than those required to produce similar lesions in the monkey or rabbit retina. This is in agreement with recent observations published by Campbell *et al*. [55]. These authors, using a ruby laser, report "the energy values necessary to produce a threshold lesion are significantly lower in rabbits than in human subjects". However, their observation that "in one human subject the threshold was lower in the macula than in other areas of the retina" is not in agreement with our observations where retinal energy densities which produced minimal lesions in the periphery failed to produce any permanent physical manifestation in the macula area. The reasons for this discrepancy may reside in the different conditions inherent in the two experiments. Campbell *et al*. [55] used a pulsed ruby laser (exposure time 0.7 ms), where Geeraets *et al*. [69] employed a high pressure xenon lamp and the exposure time was 137-140 ms. Also, the lesion sizes were quite different (our retinal image covered the entire macular area) in the two experiments; the criteria used to define minimal lesions were different, and the observation period on the patient was more restricted in our case than in Campbell's. Nevertheless, both sets of observations are encouraging and emphasize that rabbit data on retinal lesions are at lease on the safe side insofar as retinal energy density is concerned.

It must be remembered that the eyes of such patients are not free of pathology, and although the location of this melanoma was well removed from the light exposure sites, there were present in the fundus choroidal hyperemia and stromal exudates. Caution must be observed in attributing too much significance to these observations until more human data become available.

Although visual acuity was reduced slightly immediately after exposure of the entire macular area to 13 j/cm^2, recovery was complete within 15 hours. Campbell et al. also reported this slight reduction of visual acuity (20/12 to 20/20 - 3) although the lesion in their experiment was observable and located slightly off center from the fovea.

The fact that the calculated retinal dose or incident energy density required to produce a minimal lesion in the periphery was higher (from 9.6 to 12.2 j/cm^2) in the second group of exposures is not fully understood. The possible selection of a lighter pigmented area of the fundus, mild vitreous reaction following the earlier exposures, and an increasing number of cells in the vitreous associated with the preretinal hemorrhage may have been contributing factors.

Vassiliadis and co-workers(65) reported their findings of human experimental exposures. However, the ocular malignancy in their human volunteer was apparently quite advanced, thus greatly interfering with ocular transmission. This factor may have caused the widespread of required energy which caused or did not cause retinal injury. Visible lesions occurred with energy output as low as 44 μj while on the other hand 150 μj energy output did not result in a visible lesion. Though the authors tried to explain this discrepancy by possible errors in estimated spot sizes due to incomplete paralysis of accommodation as well as to vitreous haziness and possible obscuration of the laser beam by the tumor, the last two factors seem to be the most important ones. Vitreous haziness and general inflammatory reactions caused by the ocular pathology represent major difficulties in this kind of human experimentation. This factor is even potentiated by the unknown biological response to insults superimposed on the already evident pathological condition.

SUMMARY

1. In this report only measured data are used; no extrapolations are quoted or made, for such extrapolations are misleading and in many instances erroneous.

2. Ocular spectral characteristics:

   a. absorption of radiant energy by the retinal pigment epithelium and choroid in the human and chinchilla rabbit eye are similar and occur primarily in the range 400-950 nm, the peak absorption occurring at approximately 575 nm.

   b. choroidal pigmentation in the Rhesus monkey is significantly heavier than that in man.

   c. spectral transmission through the ocular media is similar for man, monkey and rabbit.

   d. spectral reflectance from the pigmented structures of the ocular fundus is approximately 3 to 5 times greater for the neodymium wavelength (1060 nm) than for the ruby wavelength (694.3 nm).

3. Ophthalmoscopic findings of minimal retinal lesions:

   a. for relatively long exposure times (millisecond-second lesions are usually smaller in diameter in comparison with the image diameter of the exposure beam on the retina. This is a heat conduction phenonenon.

   b. for short exposure times (microsecond ranges): lesion diameter is almost equal to image diameter of the exposure beam on the retina. Borders of lesions are sharply demarcated. There is no difference in appearance for lesions produced by white light or ruby laser.

   c. for extremely short exposure times (nanosecond): lesions show signs of cell disruption and subretinal hemorrhages at levels slightly above "threshold" for visible lesions.

4. Histological findings of minimal retinal lesions:

   a. for long exposures (millisecond-second ranges): coagulation effect of PE and retinal receptor cell layer is prominent with hyperemia in choroid and pyknotic nuclei. Retinal edema present in the entire neural retina overlaying the lesion.

   b. for short exposures (microsecond ranges): sharp borderlines of defect. Coagulation effect evident with involvement of PE and outer layers of the neural retina. Little or no effect demonstrable in choroid.

   c. for extremely short exposures (nanosecond ranges): disruption of PE cells and scattering of pigment granules into receptor cell layer. Free blood cells may be seen protruding through ruptures in Bruch's membrane.

5. Staining techniques, using DPN diaphorase as one possible sensitive indicator for demonstration of extent of retinal injury after light or laser exposure to various stains. Among those are Hematoxylin-Eosin, pentachrome and PAS. Also the use of acid phosphatase and phosphotungstic acid hematoxylin staining of Newcomer-fixed material has been proven useful as an indicator of retinal injury.

6. Electron-microscopic findings for mild lesions produced in microsecond ranges by white light or by ruby laser showed identical changes in PE and receptor outer segments. Borderlines between exposed and non-exposed cells are very sharp. Observed cellular changes appear to be non-specific for this type of injury.

7. Electro-phoretic techniques represent a sensitive method of evaluating thermal injury to retinal proteins; denuaturation occurs within and peripheral to the exposed retina.

8. Retinal doses for retinal injury:

a. preliminary investigations of retinal lesions produced in the chinchilla or dutch rabbit eye with white light (400 to 940 nm), very long exposure times (3 mins.), and an image size of 800 μ in diameter on the retina required an average irradiance of 6 watts/cm^2.

b. retinal doses for production of minimal ophthalmoscopic visible lesions in rabbit eyes for pulsed ruby lasers (200 μs - 2 ms ranges), and image sizes on the retina ranging from 100 μ to 1 mm in diameter, are given in various investigators within a range of 0.8 to 1.6 j/cm^2, exception: 0.16 j/cm^2, Kohtiao *et al*.(7).

c. retinal doses for production of minimal ophthalmoscopic visible lesions for q-switched ruby laser (5 - 50 ns) and image sizes of the beam on the retina ranging from 100 μ to 1 mm in diameter, are given within a range of 0.05 to 0.1 j/cm^2, exception: 0.0045 j/cm^2, Kohtiao *et al*.(7).

d. retinal doses presented for very small image sizes on the retina have to be treated with caution since inherent artifacts may result in erroneous energy for the production of minimal cellular damage. Such artifacts are twofold: 1) either the retinal image size has been underestimated; thus, the calculated irradiance per unit area is too high and 2) the required irradiance for production of a very small lesion has to be increased to give sufficient contrast for identifying these lesions clinically.

9. The primary site of retinal injury after exposure to neodymium and ruby laser wavelengths is in the retinal pigment epithelial cell and immediate adjacent structures; there is also the possibility of harmful effects on structures of the ocular media and neural retina for wavelengths in the infrared because of greater absorption.

10. The power density at the retina for production of minimal lesions is approximately 5 to 6 times higher for neogymium laser than for the ruby laser wavelength. This fact may be in part explained by the greater reflection of the neodymium wavelength (1060 nm) from the retinal pigment epithelium and lesser absorption within this layer.

11. At high power densities (MW/cm^2) delivered in nanoseconds, retinal injury may result from events other than thermal. Such effect may include ionization from intense electric field gradients, shock waves, Raman and Brillouin scattering, double photon effects, and other nonlinear effects.

12. Presenting minimal irradiances or doses for various wavelengths and exposure times for every incident on the retina rather than on the cornea has the advantage that such physical considerations as pupillary diameter, ocular transmission co-efficient and spectral absorption characteristics of retina and choroid are already incorporated in the data.

13. The threshold for biological effects from q-switched laser exposures are apparently independent of the image size of the laser beam on the retina.

14. Required energy for production of retinal lesions in the human eye appears to be significantly greater than energy levels causing retinal injury in the rabbit eye.

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CHAPTER III

LASER FUNCTIONAL EFFECTS

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INTRODUCTION

Little can be said directly of the effects of pulsed laser exposure on visual function because the unique combination of very narrow waveband and very brief, high energy flash has not often been studied. In addition to the few pulsed laser studies, there are a small number of experiments showing the effects of monochromatic light exposure on some aspects of visual function, which will be directly applicable to CW laser problems, and a fair-sized literature on the visual effects of flash exposure to stimulus fields of varying intensity. In the following, we will attempt to summarize these results and draw what tentative conclusions are possible for the present problem. It is clear at the outset that in some areas the best that can be hoped for will be to arrive at questions and inferences which will serve as hypotheses for future research.

We will divide the problem of laser functional effects into psychophysical effects and physiological effects based on differences in measurement technique. These, of course, will often be expected to show very much the same results, but due to the differing experiences and backgrounds of those interested in vision, the two types of effects are traditionally separated. Another classification might be in terms of reversible and irreversible change.

Clearly, the laser has properties which differ from other light sources in the quality, quantity, and rate of application of energy. The high energy level of laser radiation and, more important, its very high rate of emission have been shown to affect tissue in special ways. When these properties are combined with a narrow waveband in the visible spectrum, it is reasonable to expect effects of both a thermal and photochemical nature, such as selective absorption by pigments, which will differ quantitatively, if not qualitatively, from those produced by other light sources. One may also reasonably predict that the special property of coherency will produce new effects related to the hypothesized wave-guide function of visual receptors and may serve as a potent tool for testing that hypothesis. Thus, the laser offers great promise as a research tool. On the other hand, there is no evidence to date that adapting the eye to laser light below energy levels which produce pathological change will show any results different from those which would be obtained by adapting the eye to an incoherent source with the same wave-length distribution and time rate of application of energy.

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On the question of the reversible psychophysical effects of laser exposure, we will discuss the following topics: recovery time following different intensities, durations and stimulus sizes below the burn threshold, shifts in response to wavelength following exposure, after-image effects, and the relation between effect to level of pre-adaptation. For practical reasons, we will be primarily concerned with cone vision since the rods become less sensitive than the cones with relatively low levels of adapting intensity and recover much more slowly.

Functional impairment resulting from gross damage (retinal burns) may cause distortions, loss of visual acuity, scotoma in the visual fields and wavelength shifts in the color matching mechanisms; some of these will be considered below under the appropriate headings.

RECOVERY TIME STUDIES

The topic of intensity-duration-area relationships embraces much of the fundamental research in visual science. Unfortunately, most experimental results have dealt either with functional relationships at absolute threshold or increment threshold against relatively low intensity backgrounds. Also, effects within the first minute after flash exposure have rarely been studied. Only with recent emphasis on the applied problems arising from exposure to nuclear fireballs have the effects of more intense levels been explored. With consideration of seriousness of very brief loss of sight to a low-flying tactical aviator, more attention is also being paid to the study of visual response immediately after exposure.

In order to predict laser effects on vision in various tactical military situations as well as those of accidental exposure in the laboratory, we would like to know what the recovery times are for various relevant visual tasks as a function of different physical stimulus parameters. Only with adequate knowledge of these can adequate safety standards, operational and training procedures, and protective devices be prescribed.

In general, the studies using flashes of heterochromatic (white) light show that log recovery time is increased as a function of increased total energy in the adapting flash. The typical experiment has used acuity targets (e.g. Snellen letters, grids, Landolt rings) to measure vision, although the detection of light at threshold has also been used. Severin et al.[1] show that recovery time accelerates slightly as a function of increased adapting luminance for flashes of less than 5 lambert-seconds (low flash intensity). Over a middle range of up to somewhere between 100 and 500 lambert-seconds (approx. 7.0 log troland-seconds), there is a nearly linear increase of log-seconds recovery time as a function of log intensity of flash. Beyond a flash intensity in that region, there is a leveling-off or deceleration of the recovery time which is presumed to indicate that maximum possible bleaching of the photo-receptive chemicals has occurred. The data of Miller[2] in Figure 1 show the leveling-off of recovery time clearing in the region of 1 x $10^{7.4}$ troland-seconds. The data of Metcalf and Horn[3], Chisum and Hill[4], and Hill and Chisum[5] more or

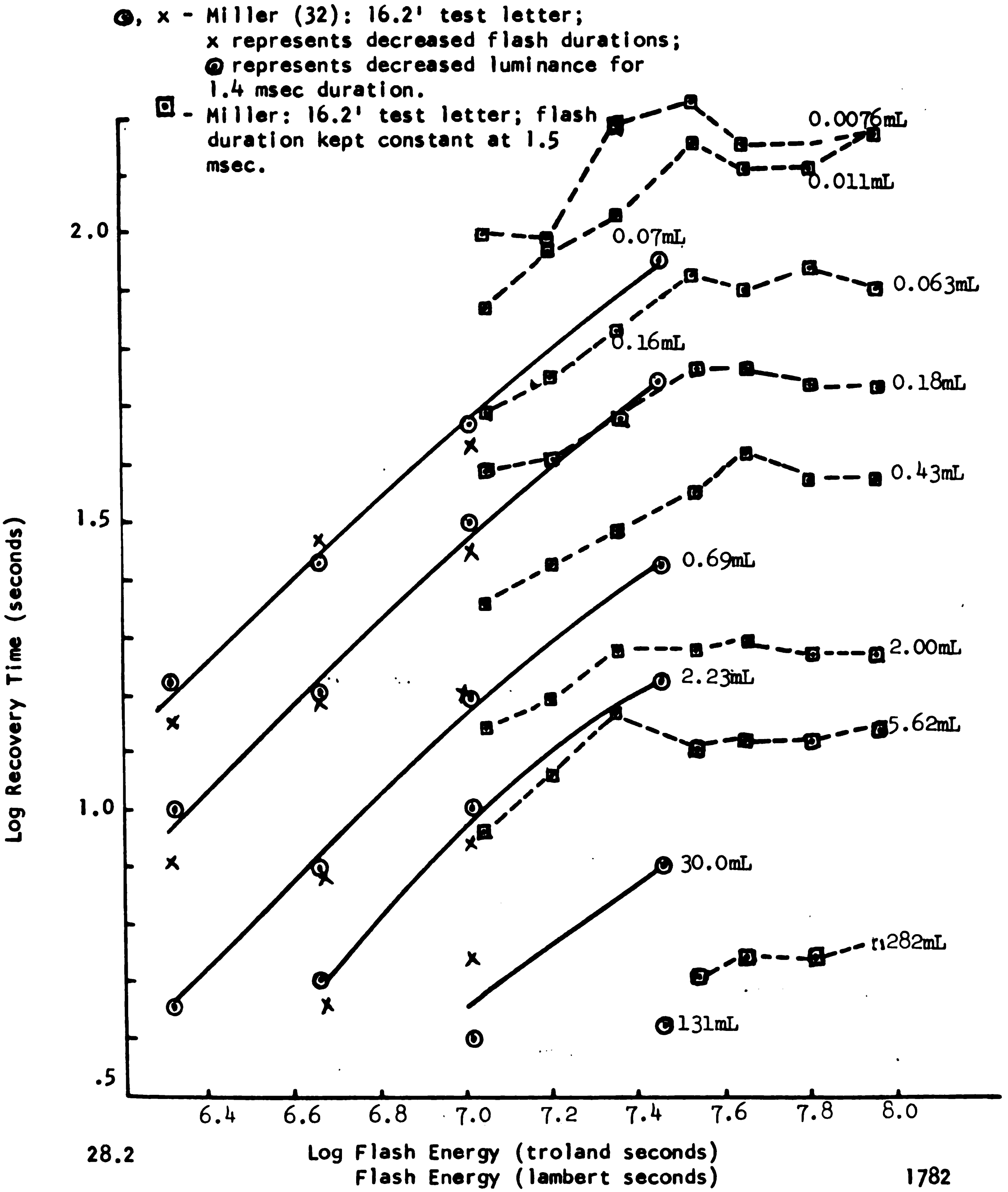

Figure 1. Recovery time as a function of flash energy and target luminance. The flattening out above 7.4 log troland-seconds (450 L-sec.) is clear. (from Czef et al. ref. 8).

less confirm Miller's findings in this regard. Above the region of 7 to 8 log troland-seconds (approx. 1 x 10^4 lambert-seconds), there is some evidence that recovery time again increases. Figure 2 shows data from Whiteside and Bazarnik[6] which illustrates this.

As shown in Miller's data in Figure 1, increased target luminance reduces recovery time. In Figure 3, this relationship shows that for three flash intensities over a range of letter-target luminances ranging from approximately 0.1 to 100 millilamberts, recovery time decreases as a negatively accelerated function from almost 100 seconds for a 3 x 10^7 trld. second flash and .1 millilambert target to only 2 or 3 seconds for a 100 ml. target. Brown[7] hypothesizes the relationship of flash energy, target luminance, and recovery time over a broad range of values to be as shown in Figure 4. He shows the positively accelerating recovery times for the lower flash energies and the approximately linear relationship over the middle range to 1 x 10^7 troland-seconds, which levels off over a range of about one log unit of adapting intensity and then accelerates toward an asymptote representing irreversible injury. This hypothetical family of functions fairly well summarizes the findings on the relationships between flash intensity, target luminance, target acuity, and recovery time for white light flashes of from .04 msec duration to 1 sec. Brown[7] and Czeh[8] have proposed predictive equations to relate recovery time to flash energy.

The recovery time-flash energy relationship has been totally unexplored for narrow-band spectral stimuli, such as those produced by lasers.

DURATION OF FLASH

A topic of great importance to the laser problem is the relationship between intensity and duration for a constant visual effect. This is the question of efficiency of light action as a function of flash duration. A number of studies of this relationship have been performed at the absolute threshold of seeing. Even those, with one exception, have not been performed over a range of narrow spectral wavebands with foveal vision. Graham and Margaria[9] and Karn[10] have shown that for peripheral rods and foveal cones the dark adapted absolute threshold is determined by total energy ($I \times t = c$) up to flashes of 0.1 second's duration for stimuli. They show an interaction with stimulus size such that as the retinal area stimulated becomes larger, the range of duration over which total energy determines the threshold becomes smaller. The "critical duration" beyond which there is a transition from total energy constant to intensity alone constant at threshold, ranges from 0.1 seconds for 2 min. diameter stimuli to .045 seconds for 45 min. diameter stimuli in the fovea. Brindley[11] has extended the intensity-time relationship at threshold to very short durations and found constancy down to 1 microsecond. Recently, Sperling and Jolliffe[12] have shown that for cone vision there is an appreciable wavelength dependency of the range over which total energy is constant at threshold. Stimuli from the short wave end of the visible spectrum summate over longer duration flashes than those composed of the

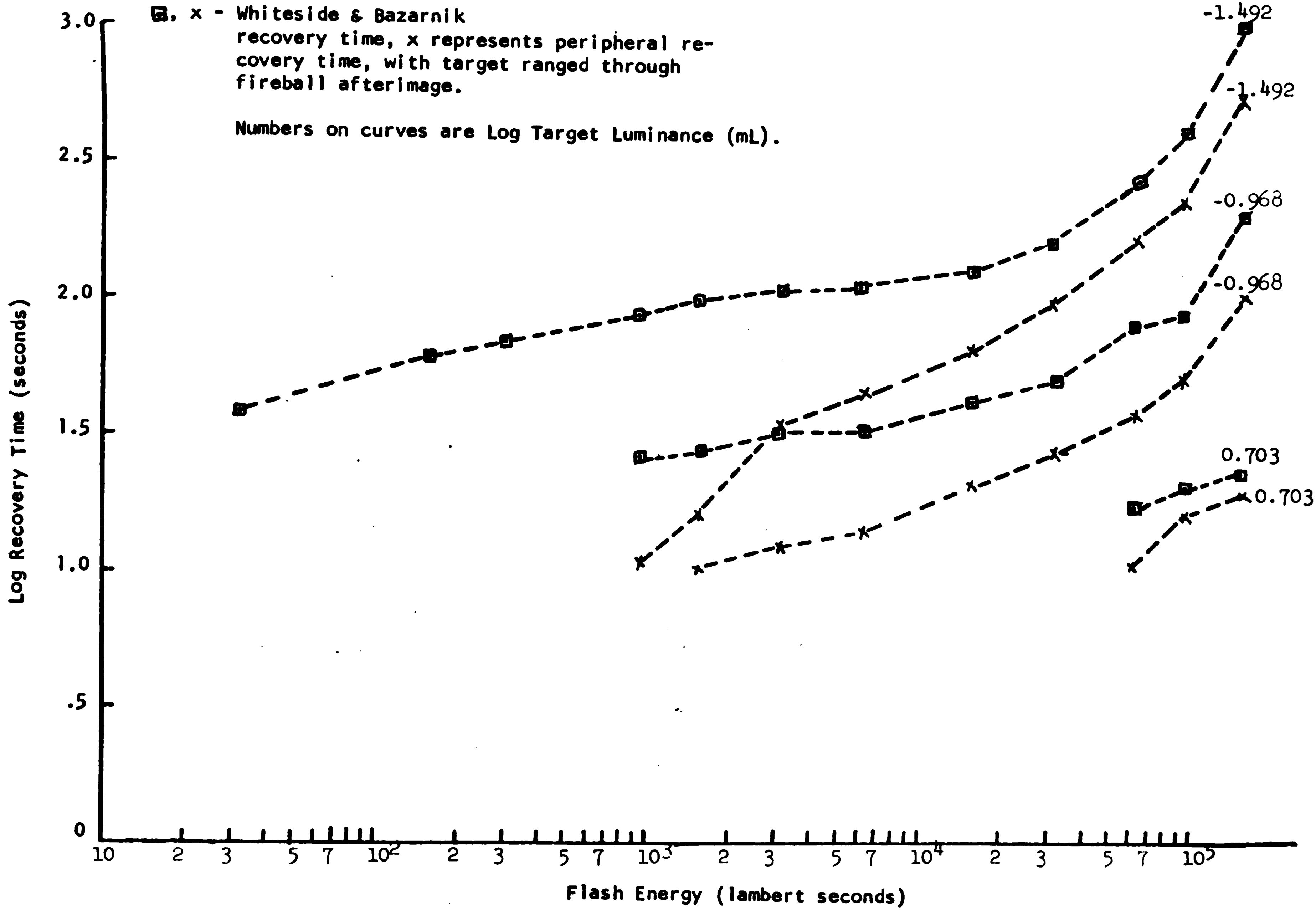

Figure 2. At very high flash energies, recovery time apparently increases very rapidly, but see text. In addition, recovery time depends on whether the target is viewed with the fovea or through the afterimage located in the parafovea. (from Czeh et al ref. 8).

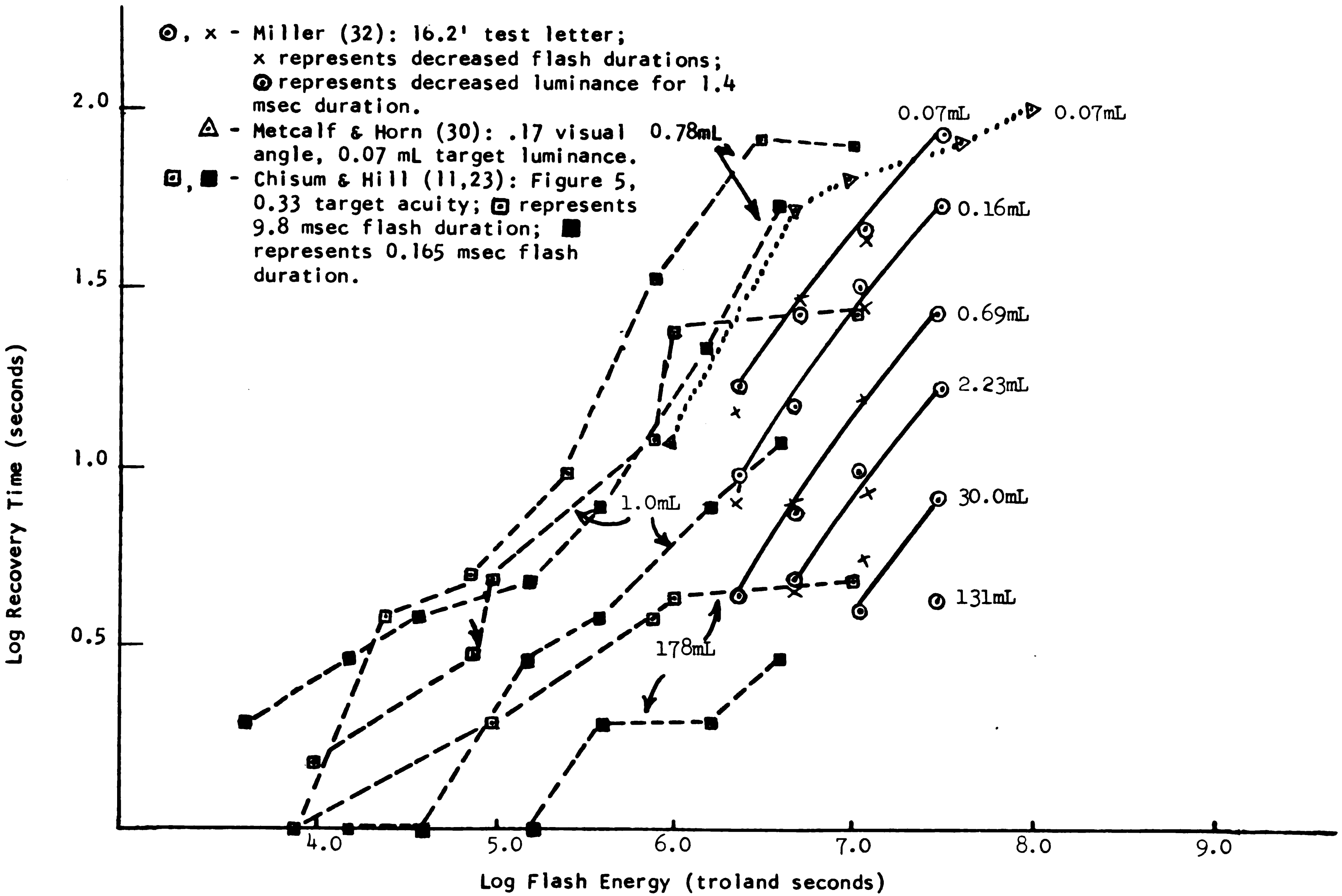

Figure 3. Recovery time as a function of flash energy and target luminance, plotted together with some of the data of Figure 5. The curves for C&H (11,23) are from Part II of their experiment, in which only the adapting flash was varied during any given experimental session. (from Czeh _et al_. ref. 8).

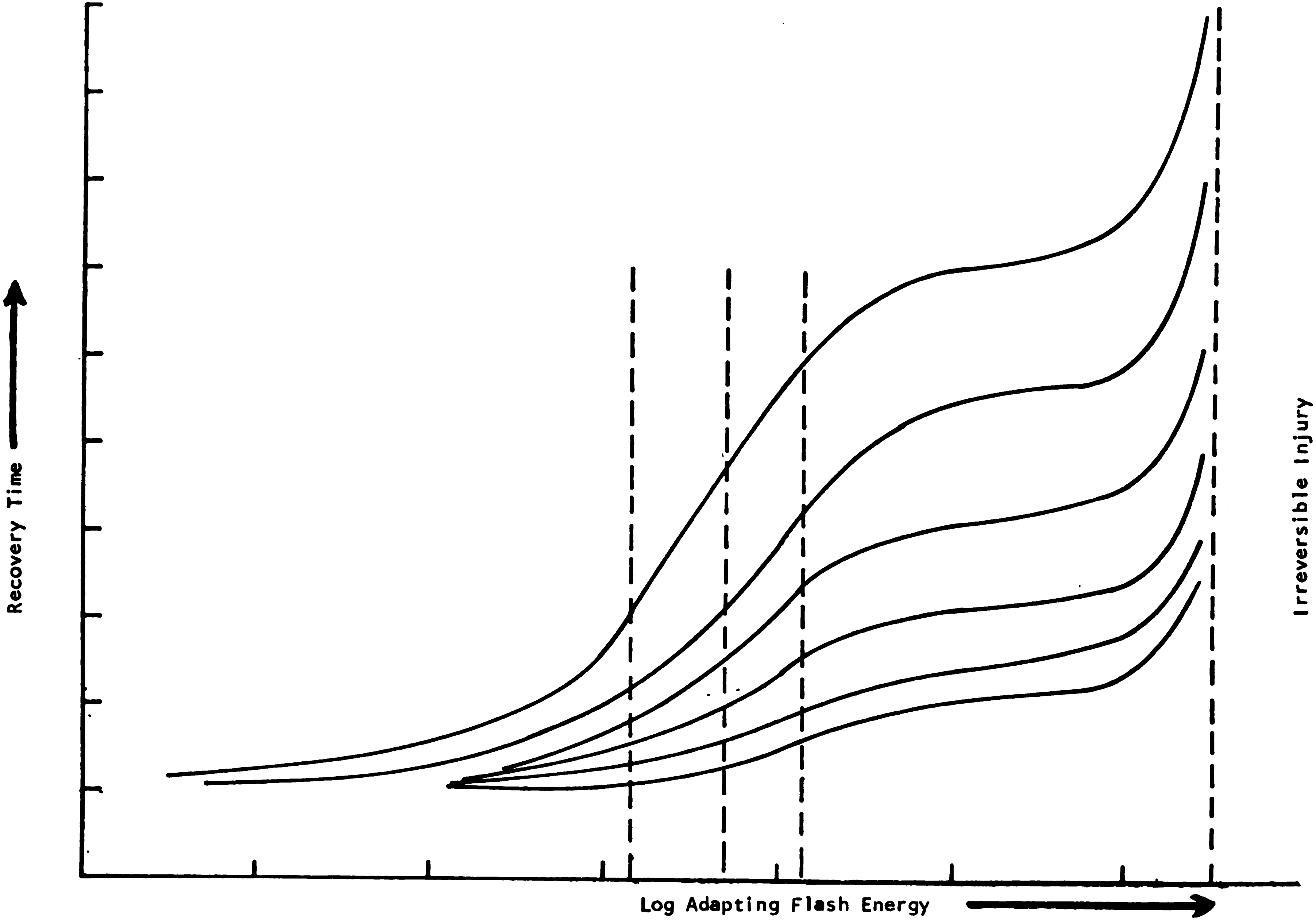

Figure 4. Hypothetical functions showing the manner in which recovery time varies with flash energy and target luminance. Target luminance increases from a low value for the curve to a high value for the bottom curve. (From Brown, 8). The effect of target visual acuity is much the same except that the bottom curve is associated with a low visual acuity requirement and the top curve with a high visual acuity requirement.

longer wavelengths. As seen in Figure 5, for 2 second's flash duration, a 650 nm red stimulus requires twice the energy to reach threshold as a 460 nm blue. These curves have been equated for the shortest duration flash.

At the opposite end of the intensity range from absolute threshold phenomena, there is a decided variation in the energy required to reach burn threshold as a function of flash duration. Here, high energy density pulses of shorter durations are more efficient than the same amount of energy delivered in a longer pulse in producing burns (see Chapter II), presumably because they give less time for heat conduction away from the burn site. Between these two extremes of threshold of seeing and burn threshold, little is known from psychophysical results.

For purely photochemical results on the bleaching efficiency of different duration flashes, as summarized by Brown[7]:

> Campbell and Rushton[13] found total energy determined amount of bleaching up to 48 seconds. For equivalent total amounts of bleaching energy, equal amounts of rhodopsin were bleached during exposures up to this duration. The minimum time investigated was 300 msec. Some evidence obtained with the same technique has been presented which would lead to the conclusion that the effects of adapting flashes of very short duration might not be as severe as the effects of longer flashes of the same total energy. Hagins[14] found it impossible to bleach more than 50 percent of the rhodopsin of the rabbit retina with flashes of less than a msec duration no matter how high the luminance. If the same amount of energy was distributed between two flashes separated by 1 or 2 seconds, it was possible to bleach up to 75 percent of the rhodopsin. Dowling and Hubbard[15] have explained this result in terms of underlying photochemical processes. A portion of certain unstable intermediate products of bleaching is isomerized back into photosensitive forms by light itself. With prolonged exposure, these are again bleached, a lesser portion has reached the maximum possible for the luminance used. Thus, complete bleaching requires both light energy and time. According to these results, when an adapting flash is of the order of 1 msec duration or less, bleaching cannot be as great as that which will occur for the same or even lesser amounts of light energy spread out more in time. One would predict that early psychophysical thresholds, meausred after a short adapting flash, would not be elevated as much as those after a longer duration. Similarly, dark adaptation following a short flash would not be equivalent to dark adaptation following longer exposure to a low luminance which results in the same amount of bleaching. A part of the dark adaptation process, hydrolysis of all-trans bleaching products, can occur during exposure to light. Hence, when a longer duration adapting light is extinguished, the process of recovery is at a more advanced stage than is the case after exposure to a short flash, even though photosensitive pigment concentrations and initial thresholds are the same. Complete recovery would take longer after the shorter flash.

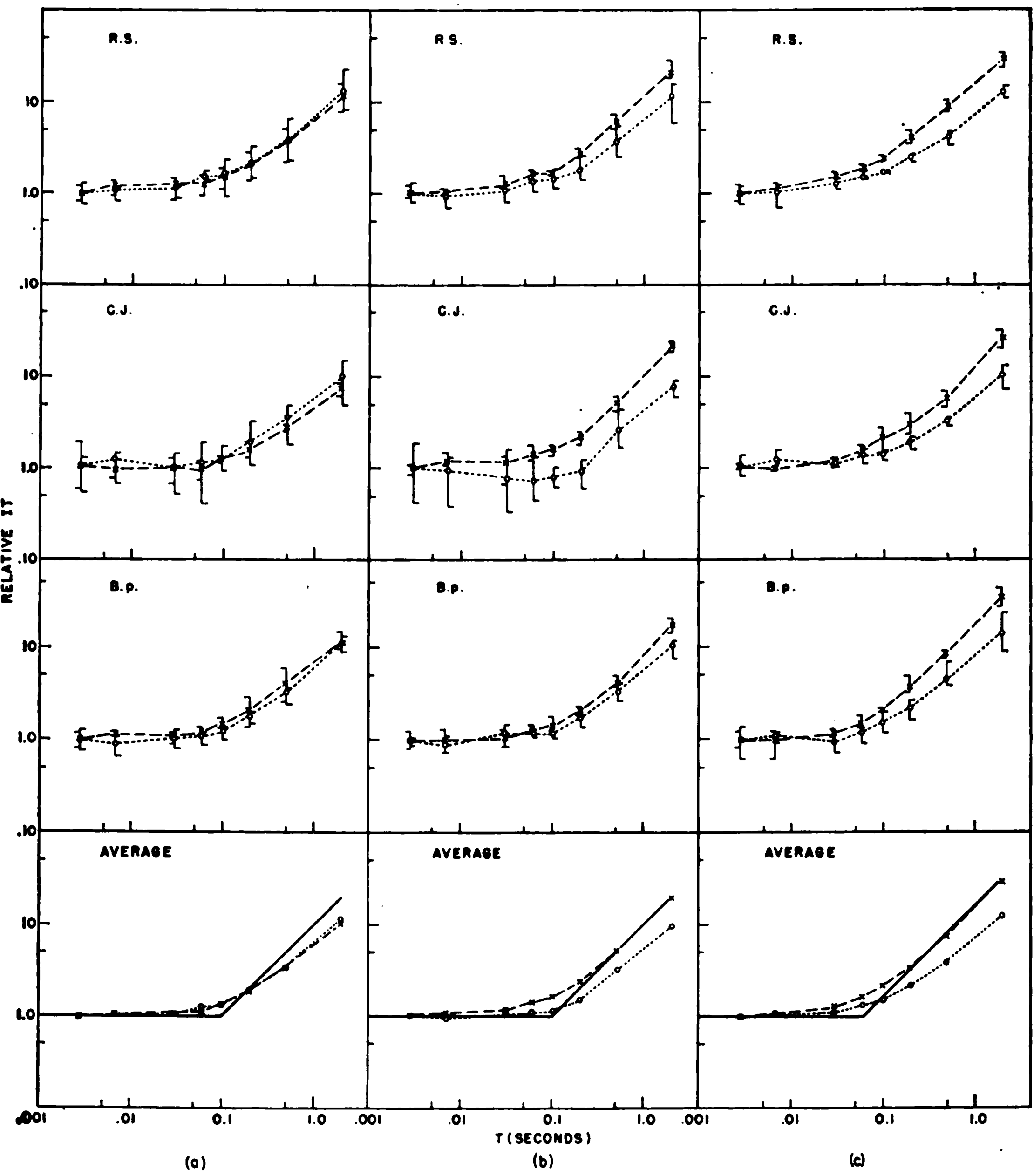

Figure 5. Relative IT values of three subjects and the subjects' average for foveal presentation. Each curve is pinned to unity at the shortest duration (0.0028 sec) to aid in the comparison of the results with two spectral stimuli. Figure 5(a) represents data with 4.5' diam stimuli and dark surround; Figure 5(b) 45' diam stimuli with a light surround (138 trolands). Data taken with the 650-mμ stimuli are represented by a dashed line with crosses and with the 450-mμ stimuli by a dotted line with open circles. Ranges of threshold determinations are included on all individual curves as brackets. A model based on Hartline's single-receptor results (solid line) is superposed on the averages. (from Sperling and Jolliffe ref. 12)

Brindley[16] has made some observations of after images which may be related to Hagin's findings. After images induced by flash luminances in excess of 3×10^6 m-candles were of the same appearance for all luminances so long as the total flash energy was presented in a short interval. The after image following a single flash was comparable to the after image of two successive flashes of the same luminance if the two were separated by only 250μ sec. If the two flashes were separated by 4 msec or more, however, there was a clear difference in the after images. The additional energy of the second flash apparently had no effect unless it irradiated the retina at an interval of several milliseconds after the first flash.

The findings of Hill and Chisum (op. cit.) may be an illustration of this kind of effect. Their curve of recovery time versus adapting flash energy indicates a more rapid recovery from a short adapting flash (165μ sec. at 1/3 amplitude) than from a long adapting flash (9.8 msec at 1/3 amplitude) of the same total energy. When the energy is distributed over a longer period, it is apparently more effective in reducing sensitivity. The experiment of Hill and Chisum is the only experiment in which extensive data on functional visual effects to high intensity adapting flashes have been obtained for flash durations both below and above a duration of from 1 to 4 msec. This is the range of durations below which Hagins and Brindley found a reduction in the effectiveness of a given amount of stimulus energy for the bleaching of rhodopsin and for the production of an after image.

WAVELENGTH SPECIFICITY OF THE ADAPTING FLASH

Little effort has been expended to study the adapting effects of intense narrow spectral bands in the visible spectrum, and no effort has been directed toward study of visual effects of adaptation to ultraviolet or infrared radiation. Burch[17] created effects similar to hereditary color blindness in human subjects with "intense color adaption". Recovery times of up to 2 hours were reported. The exact intensities used are not known, but Burch utilized the sun as a source and a 2 inch focal length lens of unspecified diameter. He used prolonged stimulation and employed broadband color filters. Apparently successive after images in addition to lowered sensitivity were found. Either of these two effects would have great practical significance for tasks utilizing vision performed after intense adaptation.

Auerbach and Wald[18] demonstrated very sizable changes in spectral sensitivity after exposure to broadband filtered red, orange-red, orange, yellow, green, blue, and white wavebands of intensities between 500 and 6,000 lumens/cm^2. Maximum dark-adapted sensitivity in the periphery of the eye (served by the rods) required up to 30 minutes to recover. The cone receptors required between 5 to 10 minutes to recover their original sensitivity. Recovery time to 50% of initial sensitivity (a crude measure of the rate of recovery) was 1 to 2 minutes. The reduction in sensivity for the cones ranged from 2.5 to 3.5 log intensity units. The studies of Brindley[19] and Cornsweet et al.[20] also employed intense spectral stimuli. Brindley's study showed that the rod (rhodopsin) and red and blue cone mechanisms are relatively more photolabile than the green cone mechanism. Cornsweet's study also demonstrated this effect, as did a more recent study by Weale[21]. These data imply that after more detailed study, eye protective devices might be specified which would provide visibility in the green region on the spectrum, and at the same time afford protection from intensities causing temporary or permanent flash blindness.

Sidley et al.[23] and Sperling et al.[24] have performed experiments in which they used very narrow-band stimuli for adaptation (2-10 nm wide) instead of the wider spectral bands (15-50 nm) which workers had previously found necessary to obtain high intensities. These studies have been especially concerned with the hitherto unexplained submaxima in the foveal sensitivity function. Early studies (Figure 6) show that there is a main peak in the function at 550 nm and smaller humps at 560-590 and 590-670 nm. Narrow-band red adaptation at 690 nm greatly reduces the hump in the red (590-670 nm), while 580 nm adaptation reduces the peak in the yellow region (560-670 nm) without eliminating the red hump. 509 nm (green) has a slight effect on the main peak, but retains both yellow and red humps. To obtain better separation of these components, more intense adapting stimuli were used, and in order to maintain a constant control condition, they were superimposed on a constant white light background of 3000 trolands. In these studies[24], data were obtained on two rhesus monkeys (Figure 7). The sensitivity data obtained with the white background light alone (Figure 7, m1 white and m3 white) were obtained in three separate blocks on each of the two monkeys. In all cases, they show an exaggerated peak in the blue at about 440-50 nm, the green at 530-40 nm, and in the orange to red at above 600 nm. The effects of adding intense narrow-band spectral lines from the red, green and blue parts of the spectrum are shown below the white light control curves for each monkey in Figure 7. Ten thousand trolands of a red, green or blue wavelength were added. Clearly, red and green intense spectral light serves to reduce sensitivity very selectively over the region of the nearest peak as seen in Figure 7A, B, C and D. Blue adaptation has a somewhat different effect, reducing sensitivity over the entire spectrum in addition to removing the peak in the blue region. Apparently, also, intense blue light reveals a peak in the 570-90 nm region, which does not show under the white light plus red, white plus green conditions. The apparent difference between intense blue adaptation and red and green is discussed in a theoretical context by Sperling et al.[24] For our present purposes, these results demonstrate that the eye's sensitivity in other spectral regions may be relatively preserved after an intense narrow-band flash, whether it emanates from a laser or a filtered incoherent source.

It appears that the effect of adding an intense spectral light to the field of a light-adapted eye is to lower sensitivity over the region of the lobe or peak in that part of the spectrum between 2x and 100x more than in the region of the adjacent peak, thus altering the shape of the spectral sensitivity function in a predictable way. These results conclusively demonstrate that calculations of the effect of intense monochromatic light exposure on vision (such as attempted recently by Zaret

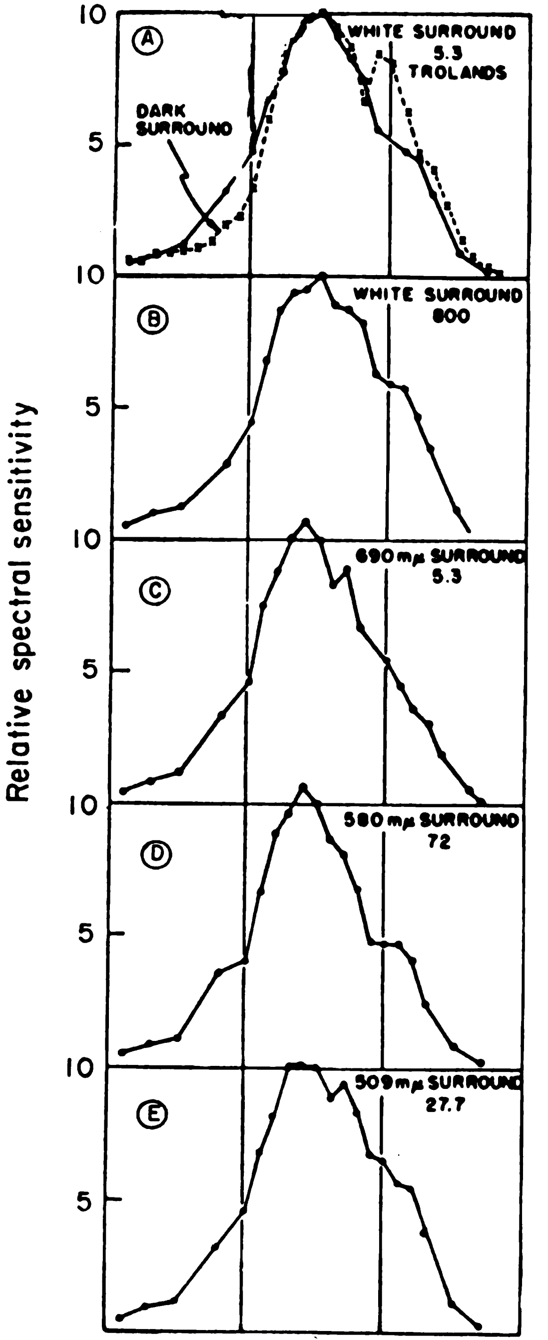

Figure 6. Relative spectral sensitivity of the fovea for different conditions of very narrow-band adaptation. A: 5-3 troland white; B: 800 troland white; C: 5-3 troland 690 mμ red; D: 72 troland 580 mμ yellow; and E: 27.7 troland 509 mμ green. Superimposed on A, as shown by crosses and dashed line, are the results obtained by Sperling and Lewis with completely dark surround.

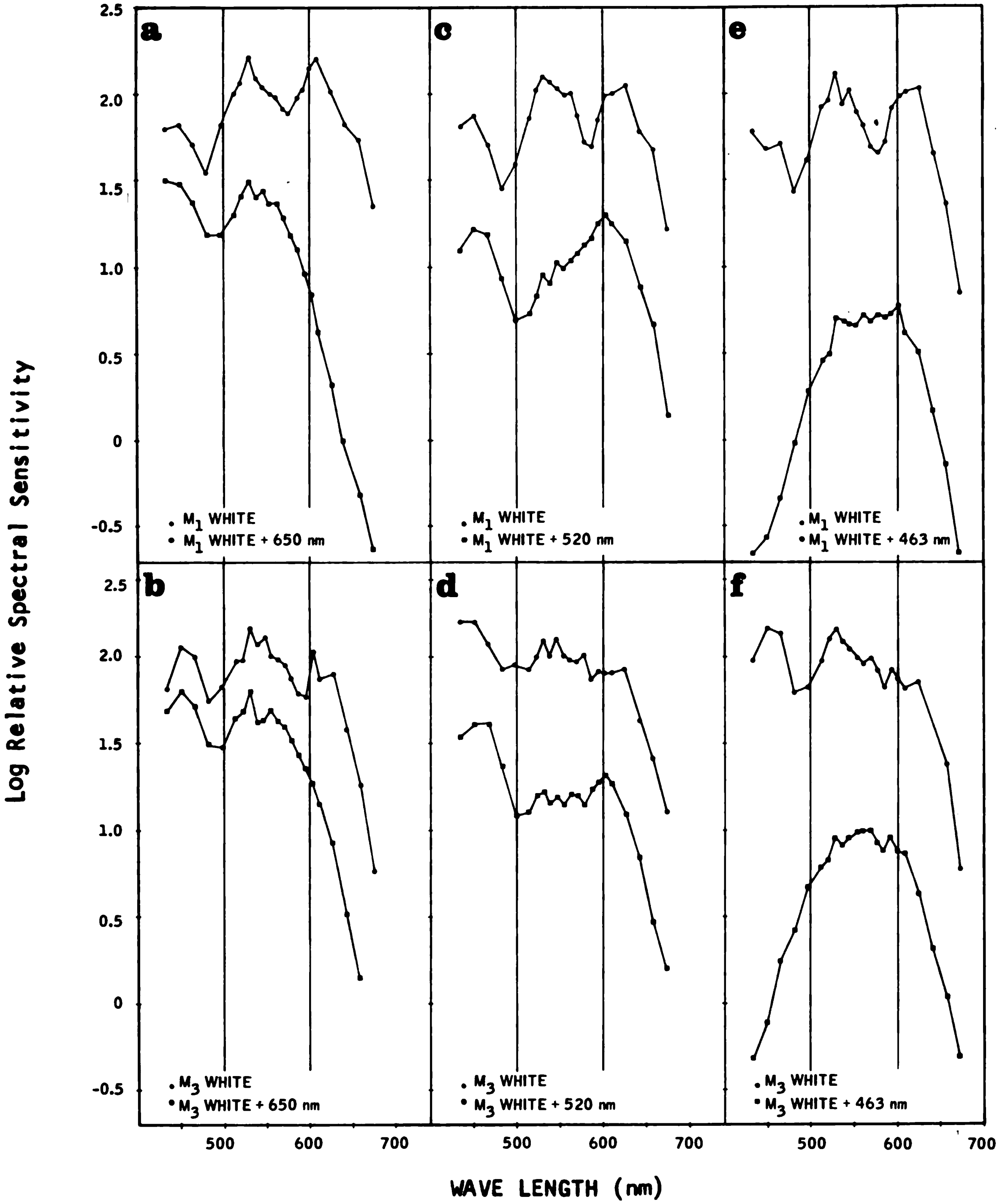

Figure 7. Log relative spectral sensitivity for white-light and white-plus-spectral-light conditions for two monkeys. Intense narrow-band 650 -nm red added to white is compared with white alone (a,b); 520-nm green plus white with white alone (c,d); and 463-nm blue plus white with white alone (e,f) (from Sperling et al ref. 24).

and Grosof[28] to compare flash blindness and burn thresholds) must not be based on a shape-invariant function such as the CIE photopic luminosity curve.

Aside from differential absorption of different wavelengths in the rods and cones, the different parts of the retina have different absorption peaks. The high intensity narrow wavelength radiation from different lasers might be expected to cause irreversible damage in different layers of the retina as the wavelength is changed. For example, Wolbarsht _et al._[29] found that the ruby laser (6943 Ångstroms) caused greater damage of the pigment epithelium and adjacent tissue, whereas the neodymium laser (10,600 Ångstroms) appears to damage the photoreceptor and neural layers at energy levels in which no histological damage could be seen in the pigment epithelium. We would expect to cause functional damage of large areas of the retina at 10,600 Ångstroms from burns on or near the optic disc involving the overlying nerve fibers. Ruby and other lasers in the visible part of the spectrum would be expected to cause little of such damage.

VISUAL ACUITY MEASUREMENTS

Since the fovea has not only the most acute color vision but also the highest spatial resolution (acuity), the majority of noticeable reversible and irreversible changes may be expected from laser exposure in this region. When the chromatic adaptation is at a level sufficient to cause deviations from normal color vision, Brindley has found that there is also a degradation of visual acuity. As Rathkey[30] and Yarczower _et al._[31] have shown, there is a marked permanent degradation of visual acuity following large laser lesions of the fovea. In this respect, much of the data already available from previous studies on retinal burns resulting from fireballs or sun viewing would be appropriate. However, the laser with its higher power density and narrower wavelength may cause lesions with special features not found in other forms of damage. The high power density could possibly cause smaller burns in the foveal area, and the narrower band wavelengths could cause selective destruction of single photoreceptor types with a permanent change, for example, in color vision, in a portion of the retina.

ERG AND LASER EXPOSURE

The electroretinogram is relatively easy to record and yields a quick assessment of the functional state of the retina. However, the typical ERG is a response of the whole retina and is elicited as much by stray light from entopic scatter as it is by direct stimulation of the retina. This was demonstrated by Asher[32] who restricted the stimulus to the blind spot and recorded normal ERGs. Detection of a small scotoma or chorioretinal burn with the electroretinogram is difficult but probably can be done with precise stimulus control and with computer averaging of a large number of responses.

Armington, et al.[33] first demonstrated that if the stimulus spot is superimposed on a large background field, the effect of stray light outside the geometrical image of the stimulus is greatly reduced. Brindley and Westheimer[34] found that a background luminance of 8.5 cd/m^2 was sufficient to eliminate the effect of light scattered from the geometrical image of the stimulus, "and to establish electroretinographic perimetry as a technique available for the investigation of local disorders of the retina."

Extreme care must be taken in the collection and interpretation of the electroretinogram if valid conclusions about the functional state of the retina are to be drawn. Several electroretinographic investigations of retinae with grossly visible lesions have found no difference between normal and damaged eyes. Ponte[35] has compared the ERG of 16 subjects with focal solar mascular injury with five normal subjects and found no differences in the photopic or scotopic components of the ERG. Jacobson et al.[36] produced focal macular destruction in monkeys with a white light photocoagulator and were unable to demonstrate any loss of photopic ERG function.

However, McNeer et al.[37] were able to demonstrate a significant decrease in the amplitude of the b wave in rabbits if a retinal area of approximately 40mm^2 was exposed with a number of "subthreshold" coagulations. The retinal energy density required to produce detectable changes in the ERG was about 50% of the retinal dose required to produce a visible retinal lesion.

Jones et al.[38] have recently demonstrated that a single ruby laser pulse of large retinal subtense (approximately 1 cm^2) at a retinal energy density of 0.2 J/cm^2 produces a significant decrease in the implicit time of the b wave and depresses the third oscillatory potential of the x wave in the Mangabey monkey. These changes parallel the kinds of changes seen in the ERG of the protanope as reported by Rendahl[39].

The value of the ERG as a diagnostic device to determine if a person has received a damaging retinal dose of intense spectral radiation is somewhat doubtful. If the exposure is to undiffused laser light in the far field, the retinal image diameter of exposure will be a diffraction limited image of 20-40μ. If retinal damage cannot be seen in a careful eye examination, the likelihood of detecting any damage with electroretinographic studies is extremely remote. On the other hand, if a large retinal area is exposed at subthreshold energy densities through multiple exposures or diffused light, significant changes in the waveform of the ERG may be detectable.

SUMMARY

Although surely incomplete, the above survey (of intense light action on the retina) demonstrates that a great deal of the evidence needed to predict laser functional effects is missing.

Little has been done on the effects of narrow-band spectral light and nothing for intensities in the laser region.

- - No attempt has been made to include the variables of adapting wavelength and intensity in studies of recovery to a useful acuity threshold.

- - No study has been reported which provides a quantitative relationship between flash duration and adapting wavelength for a functional criterion such as threshold or supra-threshold light detection or threshold acuity.

- - No work has been done on functional loss in the range of intensities between where photopigment bleaching approaches 100% and where gross burn lesions are observable. This range varies from approximately 1 to 3 log units of energy depending on the adapting and test wavelengths, duration of the flash, and retinal image size. It is, therefore, quite important that data be obtained on these variables, since a two log unit range may well be the difference between feasibility and impossibility with regard to eye protective devices.

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CHAPTER IV

PERSONNEL PROTECTION FROM LASERS AND A DISCUSSION OF EYE PROTECTIVE DEVICES

A. E. Jones*

The laser has decidedly found its place in military field operations as well as in many scientific laboratories. The laser is an increasingly used tool for the scientist, a therapeutic device for the physician, a ruler for precise measurement of length, a stimulus for the imagination of fiction writers, a production device for microwelding and drilling, and a very precise range finder for the soldier.

The quick acceptance of lasers and their rapid application to a variety of problems have placed many people in a potentially hazardous environment. Moreover, since the first ruby laser was developed by Maiman[10] in 1960, there has not been enough time to evaluate all of the medical hazards that might be present in the unique radiation of lasers. Rapid development of new laser materials in the laboratory and by the laser industry has provided laser users with highly effective wavelengths of adequate power to destroy and alter biological systems and tissues.

Hazards that exist from lasers include some unique conditions other than the radiation itself. Solid state pulsed lasers are frequently cooled with liquid nitrogen. Extremely serious "burns" can be produced by small amounts of liquid nitrogen, and the havoc that would result in a closed space if a few pounds of this coolant were spilled on the floor can be imagined.

The electrical requirements of the laser create potential environmental hazard. High power CW devices can demand power supplies producing voltages on the order of 100 KV. Pulsed solid state laser require stored charges of several hundred thousand joules. In addition to the hazard of fatal electric shock, conditions can exist in these devices which produce x-rays and become potential radiation hazards. The power is usually transmitted some distance from the power source to the laser head by cables that can be both an electrical and mechanical hazard.

Exploding components are another hazard associated with laser operation. Flashtube explosion is an occasional, if not frequent, occurrence. Most of the flying glass is confined within the cavity when a flashtube explodes, but in some systems, the end caps of the tubes are not confined and blow out with considerable force. Gas lasers can present a special hazard when broken if the gases used are toxic, for example, cyanide compounds.

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The organ most susceptible to severe laser injury continues to be the eye. While the laser beam is the primary hazard, the eye can also be damaged by the flashtube discharge and the light plume produced by laser impact on a target. The use of protective goggles is necessary in a laser environment but not sufficient to guarantee safety. Ideally, goggles should be totally opaque to the laser wavelength being used but preserve visual sensitivity throughout most of the visible spectrum. They should be lightweight and well-fitted but provide adequate ventilation for use over long periods of time. Finally, goggles should protect the wearer from the harmful brilliance of the plume. A discussion of the types of eye protective devices available and current development trends has been provided by Rob Roy MacGregor in the next section.

Many people who might be accidentally exposed to laser radiation will not be provided with eye protective devices. Considerable care must be taken in the preparation of spaces where lasers will be used. Spaces in which lasers are used should be clearly marked with distinctive warnings. Moreover, the laser beam must be contained within the marked spaces. The laser beam is capable of producing ocular damage at extreme distances. The characteristics that make the laser a suitable instrument for ranging, inherently make the instrument hazardous to a far field observer. These considerations require that the laser be so arranged in the space that the beam cannot go out an open door or window unless it is intentional. The space where lasers will be used should be painted with a flat paint of low reflectance. Where possible, draping the target area with fire-proofed black material will help to contain the glare from the plume and reflected laser radiation. A good procedure used at the Lawrence Radiation Laboratory[9] restricts the path of laser beams to heights less than five feet or greater than seven feet so that the beam will not be at eye level.

Our knowledge of potential ophthalmological hazards that exists from lasers must be extended as laser technology produces higher power devices, both CW and pulsed. The hazards from normally pulsed ruby devices appear to be primarily thermal events and are most severe in pigmented tissues, i.e., iris, pigment epithelium and choroid. Ruby energy absorbed in the iris can produce synechia, and heat conduction from the iris can be an adequate stimulus for cataract formation. Normally pulsed ruby directed to the fundus is absorbed by the pigment epithelium and choroid. If the retinal dose is on the order of 0.8 J/CM^2, visible lesions are produced. If the energy density is sufficient to produce choroidal involvement, preretinal and vitreal hemorrhages occur with disastrous effects on vision (see the discussion of "Retinal injury from laser and light exposure" by Dr. Geeraets in this volume).

Direct viewing of laser impact or the output face of a laser is seldom required. Although laser impacts from pulsed and Q-switched devices produce dramatic and drastic effects, the time sequence of the events is so short that little or nothing can be seen directly. High speed photography with framing rates in excess of 2,000/sec. is sometimes to slow to clearly elaborate the formation and travel of shock waves and other phenomena. For metal working and other applications, indirect viewing is a good solution to the problem of seeing what you are doing. In other applications, i.e., alignment of optical devices or laser surgery, direct viewing is almost required. For the case of direct viewing, a "Hazard Slide Rule for Direct Illumination" has been developed by Graham W. Flint of the Martin Company. The rationale of the rule and the parameters upon which it is based are discussed elsewhere[3]. Only a few of the basic considerations will be discussed here.

The resting eye will focus rays of light emanating from objects between the distance of 30 meters to infinity on the surface of the retina. A single point of light will present a retinal image diameter that is determined by the resolving power of the eye. Images of distant point sources are diffraction-limited images. Laser radiation in the visible region of the spectrum will be focused by the cornea and lens on the surface of the retina. There is some question about just how small the far field diffraction-limited image is, but the consensus is some value between 7 and 20 μ in diameter. The hazard slide rule uses a fixed diffraction-limited image diameter of 16 μ.

A second fixed value incorporated in the slide rule is pupil diameter. The diameter of the pupil can vary from 1.5 to 7.5 millimeters. Since there is no way in which the actual pupil diameter can be specified other than on-the-spot measurement, the pupil is assumed to be maximally dilated. This assumption is conservative and the actual energy density incident on the retina will be overestimated.

Each parameter that constitutes a variable is given a separate sliding scale. The variables considered are: 1) power in watts; 2) pulse length in seconds; 3) beam width in radius; 4) range in meters; and 5) loss factor. These factors are self-explanatory with the possible exception of the loss factor. Atmospheric attenuations over the path of the laser beam must be considered in terms of the laser wavelength and the distance involved at the time the laser is used. These data are not always immediately available to the operator, and for the sake of field utility a medium value of 2×10^{-7} CM^{-1} is used. Provision is made for taking account of an additional loss factor if the true atmospheric attenuation factor over the laser beam path for the wavelength used is known. A second use of the loss factor involves the absorption of the laser wavelength by the ocular media. The slide rule assumes a transmission factor for the ocular media of 100%. If the laser wavelength is one which the ocular media absorb a known percentage, the additional loss factor can be included. A factor also can be used if the observer is wearing protective goggles, if the attenuation factor of the goggles for the specific wavelength of the laser in use is known.

When all slides are correctly set, the safety factor for the specific set of conditions is indicated on a fixed scale at the bottom of the rule A safety factor of 1 indicates that a "threshold" retinal dose would result, meaning that damage would be produced. A safety factor of 10 is considered adequate, and the safe region of the scale is marked in green. Safety factors between 10 and 1 are marked in pink, and factors less than 1 are marked in red. Instructions in the use of the slide rule and the assumptions upon which it is based are printed on the back. The slide rule is available from the Martin Company, Orlando Division, Orlando, Florida.

The laser hazard slide rule is a useful device that allows a novice to determine a safety factor for a given set of conditions, with a minimum amount of information. However, the information required, i.e., power of the device, pulse length, beam width, range and wavelength, is seldom available for the devices found on the production line or in the field. This situation could easily be rectified by the manufacturer being required to put the information on a plaque on the device. It should be emphasized that the slide rule safety factors are intended only for direct viewing of the laser output.

Even when the rule is used for appropriate conditions, some caution must be exercised in the use of the safety factor. A safety factor of ten or greater should be considered correct only for single exposures. The rule is based on data that are very carefully controlled and verified. These data indicate the energy densities required on the retina for a given time duration to produce a visible burn in 50% of the exposures (Geeraets, this volume). Energy densities that are known to create visible lesions have a safety factor of 1 on the slide rule. A safety factor of 10 has not been shown to be safe for multiple exposures, especially if they are closely spaced in time. The situation can arise in which a pulsed laser is operating at the rate of 100 or 200 pulses per second and have a safety factor of 10 for any single pulse. Until data on the effect of multiple exposures and latent effects are available, a factor of 10 should be considered safe only for single exposures.

Finally, some consideration must be given to the laser wavelength in use. The absorption of the ocular media as a function of wavelength has been carefully determined by Ham and his co-workers[6]. If we assume a thermal model of injury, the attenuation of the laser energy by absorption in the ocular media can be determined from Ham's[6] data and incorporated in the slide rule loss factor. Most of the data collected for white light and normally pulsed ruby and neodymium doped glass lasers support a thermal injury model. Lasers using Q-switching generate lesions in which the thermal effect is compounded by many effects, i.e., acoustic or shock waves generated by transformation within a closed cavity phase, among others. Nonlinear effects may contribute to lesions produced by normally pulsed lasers also, but they may be very minimal and completely masked by the thermal events. The situation might arise in which a focused beam had high power density, but the target absorbed little of the energy because of the wavelength. This might allow the nonthermal effects to be seen in the production of tissue damage. Unlikely as this hypothesis is, it must be considered because phase transformation and other nonlinear effects have been reported by Fine, et al.[2]. Phase transformation in a closed cavity like the eye has disastrous consequences totally out of proportion to the radiant energy involved.

Laser radiation with a wavelength around 5500 Å will undergo appreciable absorption by the photopigments contained in the outersegments of the receptors. With the energy densities possible in laser beams, it is likely that 100% bleaching of the photopigments can be achieved with very short exposures, and this might result in damage to the photoreceptors themselves (see discussion of intensity-time relationships, page 35 in the third chapter). It has been clearly demonstrated that the radiant energy used so far to produce retinal lesions is primarily absorbed in the melanin granules of the pigment epithelium and choroid. Heat generated at the absorption site coagulates the overlying retina. In the case in which a greater percentage of the energy is absorbed in the photopigments, enough heat might be generated in the outersegment to damage the cell. Ruby laser radiation at 6943 Å is an inefficient visual wavelength and should be selectively absorbed primarily by the red sensitive photopigment, although such effects have never been observed with lasers, pronounced differential adaptation effects have been shown to intense spectral lights (page 41 in the third paper).

Safety factors determined with the slide rule are definitely not applicable when the observer is using an optical device. Binoculars, telescopes, and other such instruments greatly increase the energy density of the retinal image without increasing the image size, at least in the far field case.

The major concern in laser safety programs has been to establish some "threshold" value of retinal energy density and stay below it by an arbitrary factor. A threshold is a statistical value derived from some operational procedure. Obviously, if a given retinal energy density produces a visible lesion in 50% of the cases, then some lower energy density will produce a visible lesion in 25% of the cases. The threshold, in this sense, is a value referred to a percentage. Since retinal lesions are irreversible and no medical treatment can restore the damage, a safety level must exclude a higher percentage than 50% of injuries.

Ruby laser radiation impinging on parts of the eye other than the cornea have been shown to produce retinal damage, holes in the iris, hemorrhage and cataract. Moreover, it has been demonstrated that extremely high energy impacts in one eye can produce lesions in the other eye even though the eye was closed and covered with a black patch[7]. The most likely cause for this outcome is transmission of the radiation through the intervening tissues. This would imply that a very high energy impact on the face could produce retinal damage even though eye protective devices were used. On the lower end of the scale of intensities, Jones, et al.[8] have demonstrated that a retinal energy density of 0.2 J/cm^2 delivered in 1.5 ms to a retinal area of 1 cm^2 produces statistically significant changes in the implicit time and the waveform of the electroretinogram (ERG). This experiment has recently been repeated for the third time with the same outcome. The changes have persisted for six months and are presumed to be irreversible. See the third paper for a more complete discussion of these topics.

Several discussions of the hazards from lasers and personnel protection are available in the literature[1,2,4,5,9]. Safety recommendations for personnel protection from laser hazards really are comprised of some information and a lot of common sense. Workers who are unfamiliar with lasers and laser effects should be informed of the potential consequences of an accidental laser exposure to themselves and others. The individual responsible for laser safety and laser-proofing the area should explain the procedures used, e.g. counting down. Each worker should have enough indoctrination so as to be able to recognize an unsafe condition, and he should be aware of the individual safety measures that he must observe both for his own protection and the protection of others.

The responsibility for safe operation of laser devices must necessarily vary with the situation. The prime responsibility for protection against laser exposure must remain with the individual. In the field, range safety procedures should be followed. In the laboratory, the laser operator should determine that maximum safety conditions exist before the laser is fired. Fixing the responsibility for laser safety procedures is not the intent or even within the scope of this section. However, some individual should be responsible for safe operation of laser devices regardless of the unique use and situation in which the laser is being used.

The primary recommendation is that people be provided with adequate information to use the laser safely. It is proposed that this be accomplished by:

1. Explaining all of the hazards associated with laser devices.

2. Explaining the safety procedures which are in force.

3. Designating responsibility for safe operation of laser devices.

4. Explaining the individual safety measures that must be carried out.

To ensure that accidental laser exposures are kept to a minimum, some care must be taken in the preparation of spaces in which laser devices will be used. Specific procedures are difficult to propose because of the diversity of uses of lasers. For example, the use of flat black paint is recommended. However, few hospital administrators would be in favor of this color scheme for operating rooms. Obviously, some procedures must be a compromise between several requirements. The laser group at the Children's Hospital Research Foundation in Cincinnati has obviated this difficulty to a degree by developing a fail-safe occluder for personnel in the room. This goggle device is triggered by the surgeon and completely occludes the eyes of the people in the area, if they are wearing the device, for the period of the laser burst and plume dissipation. The closure period is on the order of 0.5 sec. and has minimal interference with surgical procedures. No laser burst may occur until all goggles are actuated. The master switch which closes the goggles operates a mechanical shutter in the laser beam. This system, while limiting the operator's visual field, provides unobstructed vision except for the period of the laser flash and plume dissipation. However, this system does not prevent direct or reflected exposure of other parts of the face.

Laser spaces should be clearly marked with distinctive warning signs. A number of signs have been proposed for national and international use, but at present there is no standard warning device. Laser Focus (Vol. 2:23, p. 9) has recently discussed the warning signs developed in the interest of laser safety. We currently use a modification of the sign developed at Texas Instruments Inc. Our modification is primarily a change in color scheme since the sign, as supplied, was essentially unreadable by color anomalous observers while it was read with difficulty by normal observers at moderately low levels of illumination.

Laser spaces should be provided with some sort of interlock doors to prevent a person from stepping into the room and being exposed. Such systems are frequently bothersome but well worth the bother. Laser devices as supplied by the manufacturer usually must be modified to be compatible with an interlock system. However, this is not a difficult thing to do. Where an interlock system is not feasible, access to laser spaces should be prevented without prior warning.

Visual loss due to laser exposure will undoubtedly be considered a job-connected disability. Therefore, if possible, a thorough assessment of vision capabilities and existing ocular pathologies should be made before a person is introduced to the laser environment and follow-up ophthalmological examinations should be made at regular intervals. Such a procedure is recommended in the fourth paper, page of this volume. A person who may have received an ocular laser exposure should be seen by an ophthalmologist immediately.

To summarize this discussion, there are some general rules that should be followed whether the laser device is used in a high school demonstration or as a production tool: (a) the hazards associated with lasers should be explained to the people who will be working around and with them; (b) special attention should be paid to the preparation of the spaces where lasers will be used and beam paths of the laser flash; (c) laser areas should be clearly demarked by distinctive warning signs; and (d) regular ophthalmological examinations should be carried out.

Protective goggles should be used at all times in the vicinity of active laser devices. A discussion of the types of eye protective devices available and current research trends follows.

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CHAPTER V

DEVICES FOR EYE PROTECTION

Rob Roy McGregor*

An extensive research program was undertaken by agrencies of the Department of Defense and contractor personnel in attempting to develop eye protection against the flash of a nuclear weapon, and many of the results are applicable to designing an eye protective device against laser irradiation. Some countermeasure research has been performed by the Federal Government specifically for the protection of optical components and eyes against laser irradiation, but it is classified military security information.

Devices constructed in the past have fallen into three categories:

1. Passive - Requires no activation or sensing of irradiation to function automatically.

2. Active-Passive - Requires sensing of irradiation and/or activation of defensive mechanism. May employ an auxiliary passive system, such as dichroic mirror or neutral density filter.

3. Active - Requires sensing of irradiation and activation initially and/or during exposure to irradiation.

All of the above devices should, if possible, have a very rapid response, withstand repeated attacks, be lightweight, economical, and reversible. In addition, an eye protective device should be transparent to visible radiation and opaque between the region of ruby and neodymium laser wavelengths. Since no useful purpose is served in passing wavelengths that do not contribute to vision, no need exists for an eye protective device for transmitting the infrared or ultraviolet spectra. Electronic vision systems utilizing these spectra can be electronically current-limited to protect both the system and the viewer's eyes, or protected by other means.

A review of representative devices and their operating principles indicates two general classes of eye protective devices, i.e., dynamic devices that may or may not be activated, and static devices that reflect or filter a given wavelength more than others.

Dynamic Devices

This type of device is normally transparent to visible light and increases its optical density upon exposure to an intensive light source. Methods of achieving this effect include but are not limited to:

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1. Phototropic, photochromic or thermotropic reactions to change optical density.

2. Magneto-optic or electro-optic effects to change optical density.

3. Placing a shutter in the field of view.

4. Destroying the optical path upon exposure to intense light source.

5. Using an electronic image system for indirect viewing.

Static Devices

This type of device is normally partially transparent to ambient visible light, and of high optical density for special regions of the visible spectrum. Some methods of achieving this are:

1. Selectively fixed density filter, i.e., neutral density filter.

2. Partially reflecting, partially absorbing fixed filter.

3. Combination of the above.

DISCUSSION OF DEVICES

Photoropic Reactions

Theoretically, the photoropic spectral absorption mechanism is capable of nanosecond reaction time, and, consequently, a great deal of the research in countermeasures has been undertaken in this area.

Some confusion has arisen in the use of various words, apparently interchangeably, to describe the phototropic reaction. Phototropism is a material property characterized by the material's ability to change its spectral absorption characteristics as a direct result of the absorption of quanta. Phototropism, photochromism, thermotropism, and thermochromium are used interchangeably to describe the effect. Since most of the reactions are photochromic, usage has led to describing the absorption of visible light and consequent color change as either photochomic or phototropic. Thermotropism and thermochromism describe the spectral absorption change after the absorption of thermal energy by the material.

Phtotropic reactions are reversible. The absorption of quanta by the molecules leads to vibrational or rotational twisting or photoionization, which changes the molecular configuration and changes the spectral absorption characteristics. Moreover, phototropic reactions are energy dependent, and their reaction times are a function of the incident radiation intensity and wavelength. Consequently, some phototropic materials react best to infrared, visible, or ultraviolet radiation. To date, closure times in the microsecond range have been achieved. In order to achieve the nanosecond closure times required for laser protection, however, it appears that external sensory and triggering circuits are not feasible, and the directly activated system should be pursued.

Magneto-optic or Electro-optic Reactions

It is doubtful that these reactions can be completed in the nanosecond time required for closure of a laser protective device. The Kerr-Electro-optic effect which causes a solid or fluid to become doubly refracting when subjected to a strong electric field has been successfully used to provide closure times in the microsecond range. The magneto-optic effects (Faraday and Cotton-Mouton) consist of the double refractions of light in a transparent media caused by a magnetic field. The Faraday effect is small, even for fields of the order of 10,000 gauss, and the Cotton-Mouton effect is even smaller. The low order of magnitude of the magneto-optic effect makes it success as a laser countermeasure unlikely.

Placing a Shutter in Field of View

This approach appeared to be easiest in the early stages of research to provide protection against the nuclear flash of atomic weapons. Several interestingly different methods proved to be partially successful in that they could achieve closure in several hundred microseconds. These systems relied on a sensory system to sense the flash and a triggering mechanism to activate an explosive charge actuating the closure mechanism. Another type of system, i.e., the explosive light filter system, explosively fired a carbon colloid between two lens, resulting in a partial shutter. Systems of this type normally achieve an optical density of only four in fifty microseconds or more and are irreversible, necessitating replacement of filter element after each use. Although perhaps adequate for nuclear flash protection, their optical densities are too low and reaction times too slow for laser eye protection.

Destroying Optical Path

An evaporated thin film reflecting coating was used as one of the internal reflecting surfaces in an optical system. Upon sensing of an intense light source, the film was destroyed, interrupting the optical path. This approach was too slow, resulting in closure time in excess of 50 microseconds. Antother approach of exploding a film of oil containing carbon onto the face of a prism resulted in the matching of index of refraction and consequent absorption of incident light. This method proved to be capable of an optical density of four in fifty microseconds. The general method of destroying optical path by physical reaction to a light source appears to be possible for lasers only if the physical reaction requires no sensing or triggering mechanism.

Indirect Viewing by Electronic Image System

This method is ideal for eye protection if the high cost, complexity, maintenance, and loss of resolution and depth of field can be tolerated. Since the intensity of the image cannot exceed a predetermined level, the only damage will be to electronic detector or phosphor and/or system components due to surge voltages or currents generated by the light pulse.

Fixed Filter, i.e., Neutral Density, Absorbing and/or Reflecting Systems

Several lightweight spectacle or goggle type protective devices have been developed which appear to offer excellent protection against pulsed laser sources at a relatively low cost and weight. These systems are partially transparent to the portion of the visible spectrum below the region of ruby lasers and enable the viewer to see while protecting against either or both ruby and neodymium lasers. The Jena colored glass type BG-18, made by Schott and Genossen in Germany, and distributed by Fish-Schurman Corporation of New York, is used in devices sold by American Optical Company, Southbridge, Mass. (Neodymium wavelength optical density of 11.2) and Fish-Schurman Corporation, 70 Portman Road, New Rochelle, New York (ruby wavelength optical density of 10). In addition, American Optical Company markets a mask goggle, #AO 488, with a combination of filters, AO #585, that provides protection against ruby and neogymium lasers. The effect of wearing these devices is similar to sunglasses, i.e., partial transmission in visible spectrum and not unpleasant. Some change in preceived colors occurs, of course, as the red wavelengths are absorbed and per cent transmission of the visible spectrum is less than with good sunglasses. They are not effective against high power-levels and tend to craze with continued use.

CONCLUSIONS

Although a great deal of research has been accomplished to develop eye protection against nuclear flash with some success, the only commercially available methods of eye protection against lasers today are limited to fixed filter and/or reflection type systems. Phototropic absorption offers great promise, and research is continuing to develop this method of eye protection. However, as high power lasers are developed in the visible spectrum, the vision protection problem becomes far more acute than at present. The fixed filters presently available would be inadequate unless narrow band cut-offs could be established without further reduction of visibility.

CHAPTER VI

EYE EXAMINATION STANDARDS AND TREATMENT

H. Christian Zweng* and Heinrich Rose*

EYE EXAMINATION STANDARDS

The purpose of this chapter is to set forth the outline of an initial eye examination for one who is to be placed in a laser environment and subsequent eye examinations at regular intervals thereafter. It is important that the following eye examination be carried out to establish a baseline on each eye from which all subsequent changes can be measured so that any possible laser injury can be well documented, both for the protection of the individual worker and for the firm or agency employing him. As with the introduction of any new physical modality, it is inevitable that when laser light is widely used, problems will arise either because (a) damage is claimed which has not occurred or (b) damage is occurring which is not suspected by the worker in its early stages and which must be arrested as soon as possible and guarded against for the future. Consequently, the following eye examinations incorporate standards or procedures which measure the functioning of the human eye and can be carried out in a reasonably well equipped ophthalmological center.

Three standards attempt to obtain objective information as far as possible and record such information so that even if the same examiner does not carry out subsequent visits, the information will still be set out in a form which makes it possible to ascertain whether or not a change in the patient's ocular status has occurred.

Since all the possible effects of laser energy on ocular tissue are certainly not known at this time, especially cumulative effects, the maintenance of these records on each individual is of the greatest importance. Copies of these records should follow the worker, should he change places of employment. This is true even for copies of fundus photographs which may be made.

The initial examination upon placement of a worker in a laser environment should be as follows:

1. Ocular history: The patient's past eye history and family eye history are reviewed. Any current complaints which he now has about his eyes are checked. The patient's general health status should be inquired about with a special emphasis upon diseases (e.g., diabetes, hypertension) which can give ocular problems.

2. Visual acuity: This should be tested and recorded in Snellen figures for distance with an without lenses down to 20/15. The visual acuity at near should be tested at 35 cm and recorded in Jaeger test figures with and without lenses, if any.

3. Determination of patient's lens correction with a lensometer.

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4. External ocular examination: This includes examination of brows, lids, lashes, conjunctiva, sclera, cornea, iris, and pupillary size, equality and regularity.

5. Color vision screening: This is done with the American Optical Company Ishihara color vision plates.

6. Amsler grid: The Amsler grid sheet is presented to each eye separately and any distortion of the grid is noted by the patient and drawn by him.

7. Visual fields: The peripheral visual field is charted with a 1 mm white target at 33 cm distance and a central visual field involving the fixation area is charted with a 1 mm red target at 1 meter.

The pupils should then be dilated by the instillation of one (1) drop of 1% Mydriacyl in each eye. The remainder of the examination should be carried out with the eye under this medication.

*8. Cycloplegic refraction: This is to measure the patient's total refractive error and the new visual acuity of the patient must be noted if the visual acuity is improved over the patient's old lenticular prescription or if he has no lenses at the time of the examination.

9. Examination of the ocular fundus with a direct ophthalmoscope. In the recording of this portion of the examination the points to be covered are: The presence or absence of opacities in the media, the sharpness of outline of the optic nerve, the color of the optic nerve, the size of the physiological cup, if present, the ratio of the size of the retinal veins to that of the retinal arteries, the presence or absence of a well defined macula and the presence or absence of a foveolar reflex, and any other retinal pathology that can be seen with a direct ophthalmoscope. Even small deviations from normal should be described and carefully localized.

10. Examination by slit lamp: The cornea, iris and lens are examined with this bio-microscope and carefully described.

*11. Photograph of the posterior pole of the fundus. This includes the area of the macula and head of the optic nerve and is to be taken in color film. Positive color photograph should be mounted in the patient's chart. Also, all areas of the retina which show significant abnormalities should be photographed.

*12. Examination of the retina with the slit lamp and the Goldman 3-mirror lens: This examination allows all of the retina including the periphery to be surveyed with binocularity, high magnification, and excellent illumination to give a very definite examination of the retina.

*Editor's note: Some members of the Working Group consider the starred procedures less important and have suggested that they be made optional.

The dilation of the pupil is neutralized by the instillation of 1 drop of 2% Pilocarpine solution in each eye.

This eye examination should be repeated down to intervening twelve months.

If any ocular symptoms are present, or if the worker is in a position of special laser hazard, he is to come in immediately for examination and treatment by an ophthalmologist.

The last eye examination should be done upon termination of work in a laser environment.

TREATMENT OF ACCIDENTAL LASER DAMAGE OF THE EYE

At the present time with wavelengths available, the retina appears to be the ocular tissue most sensitive to injury from laser radiation. Since the macula is responsible for sharp central vision, it is this central portion of the retina which must be most zealously examined in cases of suspected laser injuries to the eye. If areas of the retina outside the macula are injured by laser irradiation, effect on vision will in most cases be negligible, but even small injuries to the macula will result in visual loss. Until further evidence is accumulated, laser burns of the macula will best be treated as thermal effects and treatment should be effected with anti-inflammatory agents.

At this time, therefore, it is recommended that any patient receiving macular injury from laser irradiation in the acute phase be treated with cortical steroids in maximal doses compatible with usual restrictions necessary in using these agents upon human beings. Treatment should be instituted promptly and since evidence of healing persists for several weeks in the form of increased pigmentation, treatment should be carried on for at least that length of time. For the first two weeks after injury, the patient should be examined and evaluated daily; for the next one month, weekly; and for the following six months, monthly.

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	ROLE	WT	ROLE	WT	ROLE	WT

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