Chapter 37

Light Toxicity in the Posterior Segment

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It has long been known that light can cause damage to the posterior segment of the eye. What is the nature of solar damage to the eye and how has the notion of light-induced retinopathy evolved into the concepts recognized today?

Light interaction with the retina can result in various tissue effects. The three ways in which light can damage the posterior segment of the eye are photodisruption, photocoagulation, and phototoxicity.¹

Retinal photodisruption is a form of mechanical damage caused by high-powered, ultrashort light exposures, usually nanoseconds to picoseconds in duration. The target tissue is disintegrated and the adjacent tissues are disrupted by shock waves.² Photodisruption of retinal tissues usually occurs accidentally in conjunction with Q-switched laser use.³

Retinal photocoagulation is a form of thermal damage caused by high-powered, short light exposures, usually between 0.1 and 0.5 seconds in duration.⁴,⁵ The target tissue is heated, and the rise in temperature of the affected tissue causes cellular damage, including coagulative necrosis, with subsequent scarring.⁶ Permanent damage can occur when the temperature is raised by as little as 10°C.¹ Photocoagulation of retinal tissues is used clinically, with argon and other lasers. The laser burns produced by these instruments are seen almost immediately.⁷

Retinal phototoxicity results from a chemical reaction.⁸ It is caused by low-powered, relatively long light exposures, usually >10 seconds in duration.⁹ Unlike photodisruption (mechanical) and photocoagulation (thermal), phototoxicity can occur after exposure to a nonlaser light source, such as sunlight.¹ The light leads to cellular chemical reactions, with subsequent retinal damage.¹⁰ The energy required to cause this phototoxic reaction is related to the wavelength of the incident light.¹¹ Phototoxicity occurs at temperatures much below that seen in photocoagulation.¹⁰,¹¹,¹²,¹³,¹⁴ Clinically, the lesion usually is not detected until 24 to 48 hours after the insult.¹⁵

Phototoxicity can be divided into photo-oxidative (photochemical) damage and photosensitized reactions. Most toxic reactions discussed here are related to photo-oxidative interactions between incident light and various retinal tissues.¹ Photosensitized reactions include photodynamic reactions, such as used therapeutically in photodynamic therapy with verteporfin (Visudyne, Novartis, Basel, Switzerland) for exudative age-related macular degeneration (AMD).¹⁶

History

Light-induced retinal damage has been recognized at least since the time of Plato.¹⁷ Galileo reportedly sustained retinal toxicity while using a telescope for solar observation.¹⁸
In 1912, Birch-Hirschfeld suggested that eclipse blindness was caused by visible light. 19 Verhoeff and Bell opposed this explanation and, in 1916, proposed that solar retinopathy resulted from thermal damage rather than from the photochemical effects of light. 20 In 1962, Vos, using mathematical models, estimated that the temperature rise in the retina during exposure to light in cases of eclipse blindness was only about 2 degrees higher than ambient temperature. 21 Similarly, Noell et al. proposed a nonthermal phototoxic mechanism for light-induced retinal damage. 22

In the mid-1970s, Cain et al. used thermocouple probes to demonstrate that solar retinopathy occurred from photochemical damage (phototoxicity) rather than from thermal damage (photocoagulation). 23,24 In 1983, McDonald and Irvine reported the first cases of iatrogenic phototoxicity in patients who had undergone uncomplicated cataract surgery. 8 In 1986, Robertson and Feldman established a cause-and-effect relation between the operating room microscope and retinal phototoxicity. 25 Since then, numerous publications on iatrogenic phototoxicity have appeared, describing cases associated with cataract surgery, 26,27,28,29,30,31,32 other anterior segment procedures, 33,34 and pars plana vitrectomy (PPV). 35,36,37

Protective Mechanisms

The retina is protected from light toxicity through a variety of adaptations, including physical barriers (eyebrow ridge) 38 and various reflexes (squint reflex, blink reflex, and miosis). 39 Retinal xanthophyll and melanin pigments may offer additional protection, 40,41,42 possibly by converting light to heat, and by suppressing free radicals and photosensitized molecules. 12,43 The constant turnover and renewal of rod and cone outer segment discs may also blunt the effects of light toxicity. 44 Various biochemical pathways may scavenge toxic molecules, such as superoxide, hydrogen peroxide, hydroxyl radical, and singlet oxygen. 45

The wavelength and intensity of light that can be transmitted through the ocular media determine the potential for light-induced retinal damage. 46 The wavelength of visible light ranges from 400 to 700 nm. 47 Ultraviolet (UV; 100 to 400 nm) and infrared (from 700 to >10,000 nm) light represent nonvisible light adjacent to the extremes of the visible spectrum, and these, as well as the visible spectrum, are capable of interacting with the eye. 1

The cornea reflects most of the light not perpendicular to its surface and absorbs incident light in the UV-C (100 to 260 nm), UV-B (260 to 315 nm), and infrared (>700 nm) ranges. The lens absorbs most of the light in the UV-A (315 to 400 nm) range and some UV-B and near infrared light. 1,27,48 Its filtering action varies with age-related changes in lens proteins. 49 With aging, the lens provides increasing amounts of protection from shorter wavelengths. The aqueous humor absorbs some UV-B, UV-A, and infrared light, 50 whereas the vitreous absorbs light in the range of up to 300 nm and some infrared light. 51 Early poly(methylmethacrylate) (PMMA) intraocular lenses (IOL) transmitted UV and visible light. 1,52 Since 1986, most IOL designs have blocked UV wavelengths. 52

The net result is that the ocular media allow transmission of light with wavelengths between about 400 and 1,400 nm (Fig. 3-37.1). 46,49,53,54 Of particular concern are the violet (400 to 440 nm) and blue (440 to 500 nm) wavelengths.
Figure 3-37.1. A comparison of the transmittance through the ocular media (cornea, aqueous, lens, and vitreous) and the wavelength (nm) as measured for 32 human eyes, nine rhesus monkey eyes, and 48 rabbit eyes. (From Ham WT, Mueller HA, Ruffulo JJ et al: Solar retinopathy as a function of wavelength: Its significance for protective eyewear. In Williams TP, Baker BN [eds]: The effects of Constant Light on Visual Processes. New York: Plenum Press, 1980:319-346, with permission.)

Risk Factors

In general, the four most important factors in determining biological tissue response to light exposure are the size of the area affected (optical zone), the wavelength of incident light, the duration of exposure, and the total energy exposure. With regard to the retina, two important exceptions to this general principle exist, both of which are related to the unique light-focusing properties of the anterior segment of the eye. First, the optical zone is typically limited to the macula, so in effect the most important factors are wavelength, intensity, and duration. Second, a light exposure insufficient to cause damage to any other part of the body can cause significant damage to the macula.

Photochemical (phototoxic) damage is generally caused by shorter wavelengths of visible light. The most potentially toxic wavelengths are in the near-UV (320 to 400 nm) and short wavelength visible (400 to 500 nm) light ranges. In contrast, thermal injury (photocoagulation) is generally caused by longer wavelengths.

Additional risk factors for phototoxicity, demonstrated in various experimental models, include increased
core temperature^{66,67} elevated blood oxygen levels,^{12,42,68,69} and the lipofuscin constituent A2E.^{70} Potential clinical risk factors include diabetes mellitus^{28} and use of hydrochlorothiazide,^{28,71} St. John's wort,^{74} and perhaps certain IOL designs.^{9}

Clinical Manifestations

Posterior segment light toxicity is probably under reported, because many cases are asymptomatic and objective signs may be subtle. The macular changes may be more evident on fluorescein angiography than clinically (Fig. 3-37.2)

![Figure 3-37.2. A: Fluorescein angiography of a 49-year-old patient with a malignant melanoma on the left iris who consented to deliberate induction of photic retinopathy by the operating microscope before scheduled enucleation of that eye. Red-free photograph of the normal posterior pole of the left eye pre-exposure. B: Late phase of the angiogram, pre-exposure, demonstrates a normal macula. C: Red-free photograph of the left eye after light exposure showing a vertically oriented lesion centered in the macula. D: Late phase of the angiogram demonstrates hyperfluorescence in the area of photic damage. (From Green WR, Robertson DM: Pathologic findings of photic retinopathy in the human eye. Am J Ophthalmol 112:520, 1991, with permission.)](http://ovidsp.tx.ovid.com/sp-3.8.1a/ovidweb.cgi)

Phototoxicity can be divided into three phases: acute, reparative, and chronic degenerative.^{15}

Immediately after exposure, there may be no obvious sign of disease. A temporary blood-retinal barrier dysfunction may be detected by fluorophotometry, however.^{75} The first clinically apparent signs are typically mild pigmentary changes, retinal edema, or both, usually within 24 to 48 hours.^{15} The pigmentary changes may become more visible over the first week. After the first month, the lesions generally become smaller, to a variable degree.^{15,76,77} Chronic decompensation of the blood-retinal barrier can occur over years.^{7}

Light-induced retinal damage can be permanent,^{22} but typically improves to a variable extent.^{42} In general, the prognosis is fairly good.^{30,31,78,79} Important prognostic factors include the size and location of the lesion.^{7,36} Secondary choroidal neovascularization can develop.^{78,80}
The clinical syndromes can be separated into those attributed to ambient light and those to iatrogenic causes.

**Solar Retinopathy**

Solar retinopathy has been recognized for centuries, under the terms eclipse blindness, photoretinitis, photomaculopathy, and foveomacular retinitis. Solar retinopathy has been described in military personnel, sun bathers, religious sun gazers, solar eclipse viewers, and people under the influence of psychotropic drugs. Solar retinopathy is typically photochemically mediated (phototoxic), but can be enhanced by thermal effects (photocoagulation).

Typically, symptoms begin several hours after exposure and can include periorbital ache, decreased vision, metamorphopsia, chromatopsia, central or paracentral scotomata, and afterimages. Visual acuity may be reduced to 20/200, but may return to 20/40 or better within 4 to 6 months. The associated symptoms can persist indefinitely.

A small, yellowish foveal lesion may be seen in the acute phase, which corresponds to the retinal image of the sun, approximately 160 μm in diameter. As the lesion fades, it usually is replaced by a lamellar hole and may show a corresponding window defect on fluorescein angiography. Alternatively, the angiogram could be normal.

**Welder’s Maculopathy**

Welding arc exposure is typically associated with photokeratitis; however, retinal damage can occur. Clinically, welder’s maculopathy is similar to solar retinopathy. Macular hole formation can occur in severe cases.

**Operating Microscope Toxicity**

Operating microscope toxicity was suggested in 1977, with the first cases reported in 1983. Since then, this entity has become commonly recognized and is associated with various surgical procedures (Fig. 3-37.3). The first apparent report of phototoxicity during cataract surgery in a pediatric patient was published in 2004. The incidence of reported cases, specifically of iatrogenic causes of retinal phototoxicity, vary between retrospective and prospective studies.
Figure 3-37.3. A: Fundus photograph of a 58-year-old patient 1 week after uncomplicated cataract extraction with posterior chamber intraocular lens placement in the left eye utilizing a temporal clear corneal incision. The photograph demonstrates an elliptical area of pigment mottling with a yellow-white appearance at the level of the outer retina (small arrows) and with an overlying neurosensory retinal detachment (curved arrows). B: Red-free photograph of the same patient shows a lighter appearing elliptical area (arrows) at the level of the outer retina. C: Transit phase of the angiogram demonstrates a sharply circumscribed elliptical area of mottled hyper- and hypofluorescence at the level of the retinal pigment epithelium. D: Late phase of the angiogram demonstrates progressive hyperfluorescence and accumulation of dye in the neurosensory detachment. (From Dick JSB II, Bressler SB: Unusual case of postoperative phototoxic maculopathy. The Wilmer Retina Update 4:58, 1998, with permission.)

In general, the shape and size of the retinal lesion caused by the operating room microscope are dependent on the light source or filament used and the orientation of the illuminator. The shape of the macular lesion may correspond with the shape of the microscope light source. The surgeon's view through the microscope is that of diffuse, even light through one illumination source. The retina of the operative eye, however, is exposed focally to illumination from side sources of light. By design, most operating microscopes are not absolutely coaxial, so the illumination and viewing systems are not necessarily in line. The increasing popularity of topical anesthesia, with the surgeon's instructions that the patient fixate on the light source, may increase the risk.

**Endoilluminator Toxicity**

A related toxicity is associated with various endoilluminator probes used during PPV (Fig. 3-37.4). As compared with traditional halogen or metal halide light sources, the newer xenon light sources emit light at higher intensity and shorter wavelengths. They are typically used with a
bandpass filter to reduce UV transmission. In a recent experimental model, the xenon/bandpass light showed comparable toxic potential to halogen light.

Figure 3-37.4. A: Fundus photograph of a patient after macular hole surgery in the left eye. Partial closure of the macular hole resulted in more severe light-induced toxicity in the temporal macula, where the hole was closed. B: Arteriovenous phase of a fluorescein angiogram of the same patient shows a corresponding area of mottled hyper- and hypofluorescence. (Courtesy of Jay S. Duker, MD, Boston, MA.)

The increasing popularity of indocyanine green (ICG) dye to stain internal limiting membrane, epiretinal membrane, and other structures during PPV raises other potential concerns about toxicity. The absorption spectrum of ICG overlaps with the emission spectra of common endoilluminators, and a cumulative toxicity between ICG and an 805-nm diode laser has been noted in other experimental systems. Recent experimental models of ICG-mediated phototoxicity have reported conflicting results. The incidence of clinical toxicity, however, appears low at this time.

Possible Associations

Many other diseases, which are multifactorial in etiology, may include some contribution from phototoxicity. In most cases, the precise mechanisms are poorly understood and the associations are unproved.

Age-Related Macular Degeneration

A possible link between ambient light exposure and AMD was initially proposed in 1920. More recently, the possible protective effects of nuclear sclerotic cataract and ocular pigmentation have been noted. Epidemiologic studies on the association between ambient light exposure and AMD have reported conflicting results.

Similarly, an unproved potential association exists between cataract surgery and advanced AMD. Recently, it was proposed that some of this association may be caused by operating microscope phototoxicity.

Retinopathy of Prematurity

Retinopathy of prematurity (ROP) has many risk factors, primarily supplemental oxygen therapy. Theoretically, light exposure may play a role through the generation of free radicals in the retina.
The LIGHT-ROP study, in which researchers randomized >400 infants with birth weights <1,251 g and gestational ages <31 weeks to exposure to normal nursery conditions versus wearing goggles that reduce visible light and UV light, reported that ambient light did not affect the incidence of ROP in their study population.

**Cystoid Macular Edema**

A possible contributing effect of the operating microscope to postoperative cystoid macular edema (CME) has been proposed. Multiple studies have failed to demonstrate an association between UV filters on the operating microscope and CME. Conflicting results regarding the benefit of UV-blocking IOL designs have been reported. The operating room microscope emits little light in the UV range, however, and further investigation may be warranted into other wavelengths of light, such as visible blue.

**Uveal Melanoma**

The increased incidence of uveal melanoma among the white population has led some to theorize a racial predisposition related to the oncologic effects of sunlight. Some studies have demonstrated higher rates of uveal melanoma among susceptible populations, such as those living in Australia. Other reports suggest an occupational risk among those exposed to intense UV, including welders. Additional studies and a meta-analysis of over 133 published reports, however, have yielded inconsistent results and no clear association between sun and UV light exposure with the development of uveal melanoma.

**Pathologic Findings**

Clinicopathologic correlations of photic retinopathy have been reported by several investigators. An animal model of phototoxicity was developed using an indirect ophthalmoscope. Significant changes were produced the first week after exposure, but a distinct maculopathy became evident only after an extended follow-up (5 months). The authors described three stages: initial degeneration in the first week, macrophagic response between the first week and first month, and repair and regeneration between the first and fifth month. Regeneration of photoreceptors was noted over proliferating retinal pigment epithelial (RPE) cells.

Histopathologic study of photic retinopathy in the human eye caused by exposure to light from the operating room microscope was reported in 1991. A patient with an iris malignant melanoma, scheduled for enucleation, consented to exposure to an operating microscope for 60 minutes (Figs. 3-37.5, 3-37.6, 3-37.7, 3-37.8). The enucleation was performed 72 hours after light exposure. Findings occurred mainly at the level of the RPE and photoreceptor layer and included localized necrosis of the RPE; loss of the apical villi, plasma membranes, and cytoplasmic organelles of the RPE cells; extrusion of the retinal pigment epithelial pigment granules; and extensive disruption of the outer lamellae of the photoreceptors. Swollen mitochondria were present within the photoreceptor inner segments. Although this study was designed to address the issue of acute light-induced retinal damage, the additional finding of thinned RPE cells, which apparently had migrated under injured RPE cells, suggests that a reparative process had already begun.
Figure 3-37.5. Light-microscopic appearance of an area of junction between phototoxic lesion (to the right) and normal unaffected retina and retinal pigment epithelium (to the left). In the lesion, the retina is edematous. An amorphous material is observed in the area of disrupted outer segments of the photoreceptors and the subretinal space. (From Green WR, Robertson DM: Pathologic findings of photic retinopathy in the human eye. Am J Ophthalmol 112:520, 1991, with permission.)
Figure 3-37.6. Light-microscopic appearance of photic retinopathy with edematous outer retina and the edematous irregularly thickened retinal pigment epithelium. Most of the swelling involves the photoreceptor layer where an amorphous material largely replaces the outer segments. The photoreceptor nuclei appear relatively intact. (From Green WR, Robertson DM: Pathologic findings of photic retinopathy in the human eye. Am J Ophthmol 112:520, 1991, with permission.)
Electron-microscopic view of photic retinopathy with extensive derangement of the outer segments of the photoreceptors with distention (main figure), distortion, compaction, partial disintegration of the lamellar disks, and disruption of plasma membranes. The inner segments of the cones are moderately swollen and the mitochondria are markedly distended. Inset shows details of the swollen mitochondria. (From Green WR, Robertson DM: Pathologic findings of photic retinopathy in the human eye. Am J Ophthalmol 112:520, 1991, with permission.)
Figure 3-37.8. Electron-microscopic view of photic retinopathy. The retinal pigment epithelial cells are severely damaged with loss of plasma membranes, apical villous processes, basal infoldings, and extrusion of pigment granules. Overlying the retinal pigment epithelial cells, a variably dense granular material containing fragments of outer segments is observed. (From Green WR, Robertson DM: Pathologic findings of photic retinopathy in the human eye. Am J Ophthalmol 112:520, 1991, with permission.)

Similar microscopic findings were reported in studies of sun-exposed human eyes. This similarity suggests a common mechanism between damage from ambient light or iatrogenic sources.

**Prevention**

Because the basic mechanisms and risk factors involved in retinal phototoxicity are now well understood, many forms of prevention are self-evident.

Public awareness of potential damage is paramount, and may reduce the risk of toxicity from sun gazing, observation of solar eclipses, and welding arcs.

Sunglasses have an important role in preventing light damage. Ophthalmologists should counsel patients with specific risk factors, such as aphakic patients and some pseudophakic patients, especially those with non-UV-absorbing IOL designs. A recent report recommended, however, that all pseudophakic patients wear sunglasses in bright environments. Other patients who may be at risk include those receiving any form of photosensitizing medication (including verteporfin), infants and children with clear ocular media, malnourished people or those with malabsorption syndromes, and, although unproved, individuals at risk for AMD.

Standards for sunglasses have been established by the American National Standards Institute, but
enforcement may be ineffective in certain cases. Sunglass design must take into account a balance between phototoxicity protection and the maintenance of good vision with comfortable color perception. All of the wavelengths >700 nm and <400 nm can be filtered out without having an impact on visual performance, but certain compromises must be made regarding light in the 400- to 500-nm light range. Filtering out all wavelengths <500 nm would eliminate 98% of risk for retinal phototoxicity, but blocking wavelengths between 400 and 500 nm yields a yellow hue to the vision, which is poorly tolerated. Therefore, these wavelengths of light may need to be attenuated rather than eliminated. Ideally, filtration should apply to all forms of optical devices, including spectacles, contact lenses, goggles, IOL, and diagnostic and surgical instruments (Fig. 3-37.9).

Some authors have advocated blue-blocking, as well as UV-blocking, IOL materials. Other authors have proposed, however, that this will interfere with scotopic vision in elderly patients.

Preventing iatrogenic retinal phototoxicity is more complex. Light-induced retinal damage is mostly caused...
by wavelength, exposure time, and power.\textsuperscript{4,60,61} In the operating microscope, the selective use of filters to block unneeded wavelengths of light without compromising the surgeon's view may aid in the prevention of light-induced injury. In addition, by eliminating light in the infrared range, thermal enhancement of potential phototoxic damage might be reduced. Many currently available microscopes contain an internal opaque filter to shield the pupillary aperture, which can be used during parts of a procedure in which intraocular manipulation or visualization of a red reflex is not required. Alternatively, a piece of microsurgical sponge or other opaque material can be placed on the cornea over the visual axis. Nevertheless, iatrogenic retinal phototoxicity has been reported despite these precautions.\textsuperscript{79}

The surgeon should reduce the intensity of the operating microscope to the level needed for adequate visualization. Halving the illumination intensity results in a doubling of the threshold time to a phototoxic lesion.\textsuperscript{59} Oblique illumination can be used during a case when coaxial lighting is not needed.\textsuperscript{7,60}

Exposure time should be limited as much as practicable, including the use of opaque shields over the visual axis during appropriate parts of the procedure.\textsuperscript{175,176,177,178} Phototoxicity can occur in as little as 4 to 10 minutes.\textsuperscript{59} Therefore, although the total length of the procedure is important, the key factor is the time that the operating room microscope is focused on one set location of the retina. It has been estimated that, during cataract surgery, the surgeon is not looking through the oculars for up to 20\% of the procedure,\textsuperscript{179} so the illumination could be decreased during these periods. Additionally, microscope tilt or infraduction of the globe can displace the area of maximal illumination and, therefore, place the potential site of phototoxicity outside of the fovea.\textsuperscript{63}

During pars plana vitrectomy, the endoilluminator presents an additional source of potential phototoxicity,\textsuperscript{36,37} and surgeons should attempt to minimize the incident light on the fovea.

Using the above discussed techniques, the incidence of phototoxicity may be reduced, but the most important step is to maintain a high level of suspicion regarding the potential danger of light toxicity to a patient's eye.

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