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Acquired retinal toxicity following ocular surgery and pharmacotherapy: mechanisms and clinical implications

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HIGHLIGHTS

Acquired retinal toxicity is an increasingly recognized complication of modern ophthalmic surgery and pharmacotherapy, and once clinically apparent, it is often irreversible with limited treatment options. Therefore, prevention, cautious use of intraocular and systemic agents, and early detection through advanced structural and functional testing are essential to minimize preventable vision loss.

ABSTRACT

Acquired retinal toxicity represents an important and potentially vision-threatening complication of medical therapies, surgical procedures and environmental exposures. It may result from phototoxic injury, intraocular dyes, intravitreal medications or long-term systemic drug use. Advances in retinal imaging have improved early detection. However, retinal damage is often irreversible once established. Understanding the mechanisms, risk factors, and clinical manifestations of retinal toxicity is essential for prevention, timely diagnosis and optimal patient management. This review summarizes the main mechanisms of acquired retinal toxicity, illustrates them with representative clinical cases and discusses current strategies for prevention and management.

Key words: retinal toxicity, phototoxicity, vitreoretinal surgery, intravitreal drugs, hydroxychloroquine retinopathy

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INTRODUCTION

The retina, characterized by its unique architecture, the blood–retinal barrier, and one of the highest oxygen metabolic rates in the human body, exhibits a particular sensitivity to damage from exogenous factors. While advancements in pharmacology and ophthalmic microsurgery have revolutionized the prognosis for numerous ocular conditions, they have paradoxically introduced new iatrogenic risks. Acquired retinal toxicity is no longer only a rare complication of chronic systemic therapy. It has emerged as a significant clinical challenge associated with modern vitreoretinal surgery, the use of vital dyes, and antibiotic prophylaxis. The scale of the problem is substantial ranging from slow, cumulative neurodegeneration during chloroquine treatment to rapid and catastrophic hemorrhagic occlusive retinal vasculitis. The significance of this issue is underscored by the fact that most toxic changes are irreversible, and their early diagnosis is often difficult, requiring advanced imaging and electrophysiology before changes become visible in a routine fundus examination. This paper aims to summarize the current mechanisms of toxicity and their clinical implications.

METHODOLOGY

Scientific papers were analyzed using databases including PubMed, Scopus, Google Scholar, and Web of Science databases. The review focused on acquired retinal toxicity in adults and children and synthesized findings narratively across mechanisms of retinal injury (phototoxicity, dye- and drug-induced toxicity), clinical manifestations, diagnostic imaging features, risk factors, and preventive and management strategies. Case reports, case series, and review articles were included to illustrate mechanisms, clinical presentation, and outcomes.

MECHANISMS OF RETINAL TOXICITY

Phototoxicity (light-induced damage)

Photochemical injury is the most common mechanism. Intense or prolonged light exposure (operating microscope, endoilluminator, welding arcs, or even sunlight) can generate free radicals that damage photoreceptors and retinal pigment epithelium (RPE) [1–3]. Intraoperative phototoxicity typically manifests as a foveal lesion and scotoma. Such changes have been observed following cataract extraction and macular surgery, with optical coherence tomography (OCT) demonstrating focal disruption of the outer retinal layers [4]. Phototoxic maculopathy has also been reported following vitrectomy. A case has been observed in a patient receiving systemic paclitaxel (a photosensitizing chemotherapy) who developed retinal pigment changes after macular hole surgery with intraocular illumination [5]. Paclitaxel acts as a photosensitizer by stabilizing microtubules and impairing cellular antioxidant responses, thereby increasing susceptibility of retinal cells to light-induced oxidative injury during intraocular illumination [6, 7]. Notably, young patients and those on photosensitizing agents (tetracyclines or taxanes) are at higher risk [8]. Exposure to intense sunlight may likewise result in so-called solar retinopathy, a form of photochemical foveal injury with RPE in OCT scan [9]. Photochemical retinal injury is mediated by blue light-induced generation of reactive oxygen species (ROS) within photoreceptor outer segments and RPE mitochondria, leading to lipid peroxidation, mitochondrial DNA damage, and apoptosis [10, 11]. Short wavelength light is absorbed by visual pigments and lipofuscin (A2E), which act as photosensitizers and amplify oxidative stress [11–13]. In summary, phototoxicity arises from light energy interacting with photosensitizers in the retina, and prevention depends on limiting exposure (short surgical time, low-intensity light) and identifying at-risk patients.

Intraoperative dyes

Vital dyes used to stain tissues in vitreoretinal surgery (indocyanine green [ICG], trypan blue, brilliant blue G [BBG]) can themselves be toxic if misused. ICG-assisted internal limiting membrane (ILM) peeling has been associated with RPE atrophy when excess dye is retained. In such situations, characteristic large foveal areas of RPE atrophy accompanied by optic nerve pallor have been observed following macular surgery [14]. Similar outer retinal and RPE alterations have been noted after the use of ICG at high concentrations (0.5%) [15]. ICG absorbs near-infrared and visible light, generating singlet oxygen and free radicals that induce mitochondrial dysfunction and apoptosis in RPE cells [16, 17]. BBG is generally considered safer, but can also cause damage if repeatedly applied or allowed to enter the subretinal space. Accidental subretinal seepage of BBG during ILM peeling has been observed to result in localized macular dysfunction over long-term follow-up, detectable on microperimetry and multifocal electroretinography despite preserved visual acuity [18]. BBG exhibits lower photoreactivity than ICG but can still induce retinal toxicity through lysosomal accumulation and interference with mitochondrial respiration when retained subretinally, leading to localized photoreceptor dysfunction without immediate cell death [19]. In another series, 4 eyes undergoing macular hole repair with prolonged light exposure and double staining with BBG developed profound foveal thinning and choriocapillaris atrophy [20]. Trypan blue has also been implicated. Massive intraocular staining with trypan blue during complicated cataract surgery has been associated with retinal damage consistent with ecotoxic dye-related toxicity [21]. Trypan blue induces direct cytotoxicity by disrupting

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cell membrane integrity and inhibiting mitochondrial oxidative phosphorylation in RPE and retinal neurons, with enhanced toxicity under light exposure [22]. In general, the mechanism is usually toxic photochemical enhancement or direct dye toxicity to RPE/photoreceptors. Key preventive steps are to use the lowest effective dye concentration and exposure time, thoroughly wash out excess dye, and avoid inadvertent retinal contact.

Other intravitreal agents

Besides antibiotics and dyes, other injected materials can be toxic. Non-medication substances like perfluorocarbon liquids (PFCL) and retained viscoelastics have caused acute retinal damage in case series (severe ischemia and atrophy) when contaminated or left in the eye [23]. The most severe cases have been linked to contaminated perfluoro-octane, in which intraoperative exposure led to profound retinal ischemia with subsequent tissue necrosis [23]. These findings indicate that PFCL-related toxicity is likely mediated by direct chemical injury to retinal neurons and vascular endothelium rather than by mechanical effects alone [23]. Physicians should be aware that any intraocular substance, even improperly cleaned instruments, could precipitate toxic injury. Prompt recognition (performing vitrectomy to remove toxin) is the only available response once recognized.

Ophthalmic viscoelastic substances (OVDs) are usually inert, but retained or denatured viscoelastic in the vitreous can provoke toxicity. Using a dispersive viscoelastic to shield the retina during dye use has been reported to prevent surgical closure and cause inflammation when left behind [24]. Likewise, Amigó et al. include "denatured viscoelastic" in the list of known toxic intraocular agents [25]. In practice, any viscoelastic not fully removed can act as a nidus for sterile inflammation (toxic vitritis) or osmotic retinal edema. Careful aspiration of OVDs at surgery end is therefore essential.

Silicone oil tamponades can also injure the retina. Pichi et al. reviewed multiple cases of unexplained vision loss after long-term silicone oil and found consistent inner retinal damage. Spectral-domain OCT imaging demonstrated selective thinning of the inner retinal layers, particularly the perifoveal ganglion cell complex, raising the hypothesis of intraretinal migration or interaction of silicone oil components [26]. They theorize direct toxicity (oil particles embedding the inner retina) and indirect mechanisms (prolonged transparency causing phototoxicity or trapped inflammatory cytokines) [26]. Clinically, recent reports describe a "toxic posterior segment syndrome" after silicone: one case series noted acute retinal vessel occlusions on the day after oil injection, with only mild anterior reaction [27]. In that case, each episode resolved only when the silicone oil was removed. These findings underscore that silicone oil, especially if emulsified or contaminated, can trigger retinal vasculopathy or necrosis [27].

In the case of oil emulsions, new solvents (semifluorinated alkanes like F_4H_5) are being used intraocularly. These amphiphilic agents, for example perfluorobutylpentane dissolve silicone droplets and facilitate aspiration. Preclinical studies suggest these wash-out fluids are largely biocompatible [28]. F_4H_5 was non-toxic to retinal pigment epithelium (ARPE-19) cells and corneal endothelium in vitro, and another SFA (F_6H_8) showed no ocular toxicity even after 10 weeks in the anterior chamber [28]. In other words, current evidence indicates such agents are chemically inert to ocular tissues [28]. Nonetheless, their clinical use is recent, so long-term surveillance is needed. Physicians should use these only as directed and monitor for any unusual inflammation, as with any new intraocular substance.

SYSTEMIC MEDICATIONS

Several systemic drugs can accumulate in the retina. The prototypical example is chloroquine/hydroxychloroquine (CQ/HCQ), antimalarials used long-term for rheumatologic diseases. HCQ toxicity causes a concentric parafoveal or pericentral "bull's-eye" maculopathy with outer retinal loss. Of note, toxicity can progress even after stopping the drug. Progression of HCQ retinopathy has been observed to continue for several years after drug discontinuation, with documented worsening up to 9 years following cessation [29]. Similarly, newer case reports highlight toxicity occurring at doses once considered safe. HCQ retinopathy has been reported in a 61-year-old patient receiving 400 mg/24 h (5.7 mg/kg actual body weight), slightly above the 2016 guideline threshold of 5 mg/kg [30]. Chloroquine taken for malaria prophylaxis also carries risk. Permanent CQ retinopathy has been observed in a patient after 8 years of treatment with a cumulative dose of 125 g, despite literature suggesting a safety threshold of 140 g [31]. The exact mechanism is unclear, but these drugs bind melanin in the RPE and may disrupt photoreceptor metabolism [32]. Early signs include subtle pigment changes, while advanced cases can show widespread RPE and retinal atrophy with retinal vessel narrowing, resembling retinitis pigmentosa [33]. Other systemic photosensitizers or toxins include phenothiazines (thioridazine, chlorpromazine) which can cause pigmentary retinopathy, and emerging associations like pentosan polysulfate (a urologic agent) causing pattern dystrophy-like maculopathy [34].

INTRAVITREAL ANTIBIOTICS

Aminoglycoside antibiotics injected into the eye can cause severe retinal vascular and neural injury. Classic reports describe aminoglycoside retinal infarcts. Catastrophic retinal ischemia has been observed following intravitreal

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gentamicin administration, characterized by retinal hemorrhages, cotton-wool spots, arterial narrowing, capillary non-perfusion and subsequent retinal atrophy [35]. Similarly, macular infarction with permanent vision loss has been reported following intravitreal amikacin administration for endophthalmitis [36, 37]. Tobramycin can cause an occlusive vasculitis. Postoperative tobramycin toxicity has been associated with a "cherry-red" macular lesion, extensive retinal vasculitis, and rapid progression to optic atrophy [38]. Vancomycin is unique in causing hemorrhagic occlusive retinal vasculitis (HORV) when injected intraocularly. Case reports show painless vision loss after cataract surgery with intravitreal vancomycin, resulting in peripheral retinal hemorrhages, ischemic vasculitis and profound vision loss [39]. These toxic effects occur because high local concentrations of these antibiotics are directly cytotoxic or vaso-occlusive. There is no antidote, so management emphasizes extreme care (dosing accuracy, slow anterior vitreous injection) to avoid intravitreal delivery of these drugs [35].

CLINICAL CASE ILLUSTRATIONS

To illustrate these mechanisms, we summarize select published cases in table 1.

TABLE 1

Mechanisms of retinal toxicity – clinical case reports.

Mechanism	Author	Surgical procedure	Possible explanation	Postoperative changes	Final outcome
Operative phototoxicity	Nazari et al. [4]	phacoemulsification of cataract	microscope light toxicity	visual field – central scotoma, OCT showing small subfoveal outer retinal defect	almost full visual recovery
Drug-enhanced phototoxicity	Ruiz-Moreno et al. [5]	pars plana vitrectomy for macular hole	paclitaxel-induced photosensitization predisposing the retina to endoillumination toxicity	macular pigmentary changes, multifocal ERG abnormalities, fundus autofluorescence showing RPE disruption	persistent RPE changes consistent with phototoxic maculopathy (visual prognosis not clearly specified)
Solar retinopathy without sun-gazing	Stock et al. [9]	none	unrecognized light exposure or increased individual susceptibility leading to photic retinal injury	central metamorphopsia, OCT showing mild foveal RPE disruption (class II photic maculopathy)	gradual visual recovery over 3–9 months
Dye toxicity – ICG	Cheng et al. [14]	pars plana vitrectomy with ILM peeling using ICG	direct ICG-related retinal toxicity, potentially enhanced by surgical light exposure and residual dye left in the macular area	residual ICG postoperatively, circular foveal RPE atrophy significantly larger than the original macular hole, in some cases development of optic atrophy	permanent structural damage including enlarged RPE atrophy and, in some eyes, optic nerve atrophy
Dye toxicity – BBG	Almeida et al. [18]	pars plana vitrectomy with ILM peeling using BBG	accidental subretinal injection of BBG causing localized retinal toxicity	multifocal ERG showing localized amplitude reduction corresponding to the area of subretinal dye, microperimetry demonstrating decreased retinal sensitivity in the affected region	preserved central visual acuity but persistent focal functional macular damage over 2 years of follow-up
Dye toxicity with prolonged exposure	Soni et al. [20]	pars plana vitrectomy for macular hole with prolonged endoillumination and BBG staining	synergistic retinal damage from intense/prolonged endoillumination combined with repeated BBG exposure	marked foveal thinning and choriocapillaris atrophy	severe visual loss with final visual acuity worse than 20/800 in all affected eyes
Transient retinal toxicity from vitreous trypan blue leakage	Bacsal et al. [21]	enhanced phacoemulsification	retinal toxicity after prolonged dye (trypan blue) exposure; the dye was noted to enter the vitreous cavity from the area without clinically evident zonulysis posterior to the corneal incision	transient decrease in retinal responses, visual acuity 20/50 (postoperative day); a grade 1 relative afferent pupillary defect; a moderate bluish hue in the vitreous cavity until the fourth postoperative day; reduced foveal P1 response in multifocal ERG	at 1 month, BCVA 20/20; the RAPD had resolved, normal photopic a-wave amplitudes and near normal photopic b-wave and 30 Hz flicker amplitudes

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Hydroxychloroquine retinal toxicity	Eldeeb et al. [30]	treatment of rheumatoid arthritis with 400 mg/kg hydroxychloroquine daily for 6 years	toxicity of hydroxychloroquine	progressive central vision loss and a scotoma, visual acuity 20/40 and 20/30, bilateral bull's-eye maculopathy, a parafoveal ring of speckled hypoautofluorescence and an external ring of increased signal (fundus autofluorescence); parafoveal loss of the ellipsoid zone and outer nuclear layer on spectral domain-optical coherence tomography	irreversible central visual loss
Chloroquine retinopathy from malaria prophylaxis	Bertagnolio et al. [31]	long-term malaria prophylaxis	chloroquine toxicity at a cumulative dose of 125 g	chloroquine retinopathy	chloroquine retinopathy
Gentamicin injection	McDonald et al. [35]	intravitreal injection	lack of proper dilution	immediate retinal infarction, hemorrhages, edematous retina, cotton-wool spots, capillary nonperfusion	most eyes: NLP, neovascular glaucoma, optic atrophy
Amikacin for endophthalmitis	Almeida et al. [36]	intravitreal injection	unpredictable toxicity despite standard dosing	macular infarction	severe vision loss
Tobramycin post-glaucoma surgery	Pardines et al. [38]	glaucoma surgery (intravitreal injection)	unpredictable reaction after receiving intravitreal tobramycin	macular whitening (cherry -red spot), occlusive retinal vasculitis	optic and macular atrophy; unresponsive to steroids
Vancomycin-induced HORV following complicated phacoemulsification	Muid et al. [39]	intravitreal vancomycin for treatment of suspected endophthalmitis after complicated phacoemulsification surgery	toxic potential of intraocular use of vancomycin	profound visual loss with typical signs of HORV	no significant visual improvement
Intracameral ICG leakage during cataract surgery	Ksiazek et al. [40]	cataract surgery	posterior segment migration of dye	dark fundus, paracentral scotoma, subnormal rod ERG	VA 20/30, resolved scotoma, normalized ERG at 6 months
Solar retinopathy leading to lamellar hole	Yeh et al. [41]	none	photochemical injury	yellowish-white foveal lesions, FA leakage, RPE window defect, OCT: lamellar hole	permanent VA 6/60, persistent central scotoma
Microscope illumination phototoxicity during vitrectomy	McDonald et al. [42]	pars plana vitrectomy	intense coaxial light exposure during a critical period of clear ocular media	oval RPE lesions superior to the macula	visual acuity results varied between 20/20 and 20/100
Vancomycin-associated HORV	Witkin et al. [43]	intraocular vancomycin injection	delayed hypersensitivity reaction to vancomycin	unremarkable postoperative day 1 undilated examination, delayed-onset painless vision loss, mild anterior chamber and vitreous inflammation, sectoral retinal hemorrhages in areas of ischemia, and predilection for venules and peripheral involvement	in most cases 20/200 or worse visual acuity or even NLP, neovascular glaucoma

BBG – brilliant blue G; BCVA – best corrected visual acuity; ERG – electroretinography; HORV – haemorrhagic occlusive retinal vasculitis; ICG – indocyanine green angiography; ILM – internal limiting membrane; NLP – no light perception; OCT – optical coherence tomography; RAPD – relative afferent pupillary defect; RPE – retinal pigment epithelium; VA – visual acuity.

CURRENT KNOWLEDGE AND MANAGEMENT

The development of novel pharmacologic agents, their expanding clinical indications, and prolonged duration of therapy have contributed to a growing number of reported cases of retinal toxicity. Concurrently, advances in retinal imaging technologies have enabled the detection of increasingly subtle, subclinical retinal alterations associated with these medications, potentially facilitating earlier intervention and limiting disease progression. Nevertheless, the precise threshold at which retinal injury becomes irre-

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versible and leads to permanent visual impairment remains inadequately defined. As imaging modalities continue to evolve, retinal abnormalities are being identified with greater frequency in asymptomatic individuals; however, the clinical relevance of these findings, as well as the critical point at which drug discontinuation is necessary to avert irreversible, vision-threatening sequelae, requires further investigation [44].

When it comes to hydroxychloroquine-induced retinopathy at the earliest evidence of retinal toxicity, this medication should be promptly discontinued to limit further retinal injury and potential visual loss. Currently, there are no dietary, pharmacologic, or surgical interventions proven to prevent, halt, or reverse hydroxychloroquine- or chloroquine-induced retinopathy; thus, primary prevention through appropriate dosing and systematic ophthalmic surveillance remains the cornerstone of management. Hydroxychloroquine retinopathy is generally irreversible, and structural and cellular retinal damage may continue to progress even after drug cessation. Importantly, earlier recognition of subtle functional and structural changes is associated with a greater likelihood of preserving useful vision, though complete prevention of progression cannot be guaranteed. Given the absence of effective therapeutic options, discontinuation of offending agent – when toxicity is confirmed or strongly suspected – is essential but should be undertaken through shared decision-making with the patient and the treating physician, balancing ocular risk against the systemic consequences of stopping therapy [45–48].

Advanced imaging and functional assessment modalities, including optical coherence tomography (OCT), fundus autofluorescence (FAF), and multifocal electroretinography (mfERG), are capable of detecting the earliest structural and functional manifestation of retinal toxicity caused by hydroxychloroquine at subclinical stage. Together with the established standard of central visual field assessment (10-2 perimetry), these techniques are increasingly incorporated into contemporary screening strategies for hydroxychloroquine retinopathy. Nevertheless, an optimal standalone diagnostic test demonstrating both high sensitivity and high specificity for hydroxychloroquine-induced retinal toxicity has yet to be identified [47].

DISCUSSION

The presented material demonstrates that acquired retinal toxicity has become an important and increasingly recognized clinical problem, closely linked to advances in modern ophthalmic surgery and pharmacotherapy. The unique anatomical and metabolic properties of the retina render it particularly vulnerable to a wide range of exogenous insults. Across the mechanisms described, a consistent theme emerges: once clinically apparent retinal toxicity develops, structural damage is frequently irreversible and therapeutic options are limited. This underscores the critical importance of prevention, early recognition, and risk stratification.

Phototoxicity represents the most common and, at the same time, one of the most underestimated mechanisms of retinal injury. Both intraoperative illumination and environmental light exposure can induce photochemical damage to photoreceptors and the retinal pigment epithelium. The reviewed cases indicate that even routine and uncomplicated surgical procedures, such as cataract extraction or standard vitrectomy, may result in phototoxic maculopathy. The risk appears to be amplified in younger patients and in individuals receiving systemic photosensitizing agents. Particularly severe outcomes have been observed when prolonged light exposure is combined with the use of intraoperative dyes, supporting the concept of a synergistic "double-hit" mechanism that markedly increases retinal vulnerability.

Toxicity related to intraoperative dyes further highlights the narrow margin between diagnostic or surgical benefit and retinal injury. ICG, BBG, and trypan blue have all been associated with structural and functional retinal changes, especially when used in high concentrations, repeatedly, or when inadvertently introduced into the subretinal space. Importantly, several cases demonstrate that preserved central visual acuity does not preclude localized retinal dysfunction. Subtle but permanent defects may only be detectable through advanced functional testing, such as microperimetry or multifocal electroretinography, emphasizing the limitations of visual acuity as a sole outcome measure.

Intravitreal antibiotics constitute one of the most devastating sources of retinal toxicity. Aminoglycosides and vancomycin can induce profound retinal ischemia, occlusive vasculitis, and optic nerve atrophy, often with rapid onset and catastrophic visual consequences. Unlike phototoxic or dye-related injuries, these events typically show little or no recovery despite aggressive treatment. The phenomenon of vancomycin associated with hemorrhagic occlusive retinal vasculitis further complicates clinical management, as its delayed presentation and inflammatory features may mimic postoperative infection. These observations reinforce the need for extreme caution in the intraocular use of such agents and highlight the absence of effective therapeutic rescue once toxicity occurs.

Systemic medications, particularly CQ and HCQ, represent a distinct but equally significant category of retinal toxicity. The cases reviewed confirm that retinal damage may occur at cumulative doses previously considered safe and that progression can continue long after drug discontinuation. This challenges the reliability of fixed dose thresholds and emphasizes the importance of individualized risk assess-

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ment. Moreover, the inadequacy of traditional screening tools, such as Amsler grid testing alone, is evident. Objective structural and functional assessments are essential for detecting early toxicity before irreversible macular damage develops.

Advances in retinal imaging and electrophysiology have markedly improved the ability to identify subclinical retinal changes associated with toxic exposure. However, this progress introduces a new clinical dilemma: the prognostic significance of early or asymptomatic abnormalities remains incompletely understood. It is often unclear which findings represent reversible dysfunction and which herald inevitable progression to permanent vision loss. This uncertainty complicates clinical decision-making, particularly when discontinuation of a systemic medication carries substantial non-ocular risks.

CONCLUSIONS

Acquired retinal toxicity emerges from this analysis as a multifaceted and increasingly relevant challenge in contemporary ophthalmology. The retina's susceptibility to photochemical injury, pharmacologic toxicity, and iatrogenic damage means that even standard diagnostic and therapeutic interventions may carry significant risk. In most instances, once overt retinal toxicity becomes clinically apparent, the resulting structural damage is permanent and therapeutic options are limited. Consequently, prevention through judicious use of light, careful selection and handling of intraocular agents, accurate dosing, and meticulous surgical technique remains paramount.

Equally important is the role of early detection. Modern imaging and functional testing allow clinicians to identify retinal toxicity at a subclinical stage, offering the possibility of limiting further injury by timely intervention. Nevertheless, the lack of clearly defined thresholds for irreversible damage and the absence of a single highly sensitive and specific diagnostic test continue to pose significant challenges. In the context of systemic medications such as hydroxychloroquine, management decisions must balance ocular safety against systemic therapeutic benefit and should be made through informed, multidisciplinary discussion.

Ultimately, further research is required to clarify the natural history of early toxic retinal changes, establish meaningful risk thresholds, and refine screening strategies. Such efforts are essential to minimize preventable vision loss in an era of rapidly evolving surgical techniques and expanding pharmacologic therapies.

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References

1. Michels M, Sternberg P Jr. Operating microscope-induced retinal phototoxicity: pathophysiology, clinical manifestations and prevention. Surv Ophthalmol. 1990; 34(4): 237-52. http://doi.org/10.1016/0039-6257(90)90025-q.
2. Yang X, Shao D, Ding X et al. Chronic phototoxic maculopathy caused by welding arc in occupational welders. Can J Ophthalmol. 2012; 47(1): 45-50. http://doi.org/10.1016/j.jcjo.2011.12.001.
3. Robertson DM, Lim TH, Salomao DR et al. Laser pointers and the human eye: a clinicopathologic study. Arch Ophthalmol. 2000; 118(12): 1686-91. http://doi.org/10.1001/archopht.118.12.1686.
4. Nazari T, Jalink MB. Central scotoma following phacoemulsification surgery: A case report on retinal phototoxicity. Am J Ophthalmol Case Rep. 2025; 38: 102334. http://doi.org/10.1016/j.ajoc.2025.102334.

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5. Ruiz-Moreno JM, García-Zamora M, Ruiz-Medrano J. Retinal phototoxicity after macular hole surgery in a patient under paclitaxel. BMC Ophthalmol. 2023; 23(1): 342. http://doi.org/10.1186/s12886-023-03086-x.
6. Hofstra LS, de Vries EG, Willemse PH. Ophthalmic toxicity following paclitaxel infusion. Ann Oncol. 1997; 8(10): 1053. http://doi.org/10.1023/a:1008249230056.
7. Malcolm J, Lune Wong CO et al. Paclitaxel may be a risk factor for retinal phototoxicity. Am J Ophthalmol Case Rep. 2022; 25: 101292. http://doi.org/10.1016/j.ajoc.2022.101292.
8. American Academy of Ophthalmology. Solar Retinopathy. Section 12: Retina and Vitreous. Basic and Clinical Science Course, 2025--2026. San Francisco, CA.
9. Stock RA, Savaris SL, de Lima Filho EC et al. Solar retinopathy without abnormal exposure: case report. Arq Bras Oftalmol. 2013; 76(2): 118-20. http://doi.org/10.1590/s0004-27492013000200012.
10. Alaimo A, Liñares GG, Bujjamer JM et al. Toxicity of blue led light and A2E is associated to mitochondrial dynamics impairment in ARPE-19 cells: implications for age-related macular degeneration. Arch Toxicol. 2019; 93(5): 1401-15. http://doi.org/10.1007/s00204-019-02409-6.
11. Ouyang X, Yang J, Hong Z et al. Mechanisms of blue light-induced eye hazard and protective measures: a review. Biomed Pharmacother. 2020; 130: 110577. http://doi.org/10.1016/j.biopha.2020.110577.
12. Brunk UT, Terman A. Lipofuscin: mechanisms of age-related accumulation and influence on cell function. Free Radic Biol Med. 2002; 33(5): 611-9. http://doi.org/10.1016/s0891-5849(02)00959-0.
13. Sparrow JR, Wu Y, Nagasaki T et al. Fundus autofluorescence and the bisretinoids of retina. Photochem Photobiol Sci. 2010; 9(11): 1480--9. http://doi.org/10.1039/c0pp00207k.
14. Cheng SN, Yang TC, Ho JD et al. Ocular toxicity of intravitreal indocyanine green. J Ocul Pharmacol Ther. 2005; 21(1): 85-93. http://doi.org/10.1089/jop.2005.21.85.
15. Querques G, Prascina F, Iaculli C et al. Retinal toxicity of indocyanine green. Int Ophthalmol. 2008; 28(2): 115-8. http://doi.org/10.1007/s10792-007-9112-3.
16. Landsman ML, Kwant G, Mook GA et al. Light-absorbing properties, stability, and spectral stabilization of indocyanine green. J Appl Physiol. 1976; 40(4): 575-83. http://doi.org/10.1152/jappl.1976.40.4.575.
17. Sato T, Karasawa Y, Ishikawa S et al. Potential Phototoxicity of Indocyanine Green in Retinal Pigment Epithelial Cells after Angiography under Ambient Illumination. Oxid Med Cell Longev. 2018; 2018: 6065285. http://doi.org/10.1155/2018/6065285.
18. Almeida FP, De Lucca AC, Scott IU et al. Accidental subretinal brilliant blue G migration during internal limiting membrane peeling surgery. JAMA Ophthalmol. 2015; 133(1): 85-8. http://doi.org/10.1001/jamaophthalmol.2014.3869.
19. Abdouh M, Chen Y, Goyeneche A et al. Blue Light-Induced Mitochondrial Oxidative Damage Underlay Retinal Pigment Epithelial Cell Apoptosis. Int J Mol Sci. 2024; 25(23): 12619. http://doi.org/10.3390/ijms252312619.
20. Soni A, Parameswarappa DC, Tyagi M et al. Brilliant Blue G toxicity in macular hole surgeries: A report on combined phototoxicity and dye-induced macular damage. Semin Ophthalmol. 2022; 37(1): 117-22. http://doi.org/10.1080/08820538.2021.1928717.
21. Bacsal KM, Chee SP. Trypan blue-associated retinal toxicity post complicated cataract surgery. Eye (Lond). 2006; 20(11): 1310-1. http://doi.org/10.1038/sj.eye.6702164.
22. Narayanan R, Kenney MC, Kamjoo S et al. Trypan blue: effect on retinal pigment epithelial and neurosensory retinal cells. Invest Ophthalmol Vis Sci. 2005; 46(1): 304-9. http://doi.org/10.1167/iovs.04-0703.
23. Pastor JC, Coco RM, Fernandez-Bueno I et al. Acute retinal damage after using a toxic perfluoro-octane for vitreo-retinal surgery. Retina. 2017; 37(6): 1140-51. http://doi.org/10.1097/IAE.0000000000001680.
24. Veritti D, Lanzetta P, Bandello F et al. Viscoelastic agent retention and failed macular hole surgery. Retin Cases Brief Rep. 2009; 3(1): 77-9. http://doi.org/10.1097/ICB.0b013e318158de4f.
25. Amigó A, Martinez-Sorribes P. Toxic Intraocular Syndrome. J Ophthalmic Vis Res. 2022; 17(1): 155-6. http://doi.org/10.18502/jovr.v17i1.10184.
26. Pichi F, Hay S, Abboud EB. Inner retinal toxicity due to silicone oil: a case series and review of the literature. Int Ophthalmol. 2020; 40(9): 2413-22. http://doi.org/10.1007/s10792-020-01418-0.
27. Kumoi M, Matsuda S, Matsumoto M et al. Toxic posterior segment syndrome caused by silicone oil tamponade resulting in postsurgical retinal vascular occlusion: a case report. Am J Ophthalmol Case Rep. 2025; 39: 102404. http://doi.org/10.1016/j.ajoc.2025.102404.
28. Muuss M, Karaivanova M, Skrzypczyk L et al. F4H5 Alleviates Increased Outflow Resistance Induced by Emulsified Silicone Oil In Vitro. Invest Ophthalmol Vis Sci. 2025; 66(11): 21. http://doi.org/10.1167/iovs.66.11.21.
29. Karakosta C, Downes SM. Progressive Retinal Toxicity Nine Years After Hydroxychloroquine Discontinuation: A Case Report. Cureus. 2025; 17(12): e98674. http://doi.org/10.7759/cureus.98674.
30. Eldeeb M, Chan EW, Omar A. Case Report: Hydroxychloroquine Retinopathy. Optom Vis Sci. 2018; 95(6): 545-9. http://doi.org/10.1097/OPX.0000000000001226.

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31. Bertagnolio S, Tacconelli E, Camilli G et al. Case report: Retinopathy after malaria prophylaxis with chloroquine. Am J Trop Med Hyg. 2001; 65(5): 637-8. http://doi.org/10.4269/ajtmh.2001.65.637.
32. Souza Monteiro de Araújo D, Brito R, Pereira-Figueiredo D et al. Retinal Toxicity Induced by Chemical Agents. Int J Mol Sci. 2022; 23(15): 8182. http://doi.org/10.3390/ijms23158182.
33. Lin RC, Cantrill HL, Mieler WF. Retinal Toxicities Caused by Systemic Medications. Retinal Physician. 2007; November/December 2007.
34. Bonting SL, Caravaggio LL, Canady MR. Studies on sodium potassium-activated adenosine triphosphatase. X Occurrence in retinal rods and relation to rhodopsin Exp Eye Res. 1964; 3: 47-56.
35. McDonald HR, Schatz H, Allen AW et al. Retinal toxicity secondary to intraocular gentamicin injection. Ophthalmology. 1986; 93(7): 871-7. http://doi.org/10.1016/s0161-6420(86)33648-0.
36. Almeida LN, Canêdo MG, Almeida RN et al. Maculopatia isquêmica após injeção intravítrea de amicacina: relato de caso Macular infarction after intravitreal injection of amikacin: case report. Arq Bras Oftalmol. 2005; 68(6): 837-40. http://doi.org/10.1590/s0004-27492005000600023.
37. Doft BH, Barza M. Macular infarction after intravitreal amikacin. Br J Ophthalmol. 2004; 88(6): 850. http://doi.org/10.1136/bjo.2003.038885.
38. Hernández Pardines F, Tapia-Quijada H, Hueso-Abancens JR. A case of aminoglycosides induced retinal toxicity treated with megadoses of steroids and an intravitreal dexamethasone implant (Ozurdex(®)). Arch Soc Esp Oftalmol. 2016; 91(6): 288-91. http://doi.org/10.1016/j.oftal.2016.01.017.
39. Muid J, Awan MA. Haemorrhagic occlusive retinal vasculitis caused by intravitreal vancomycin. J Pak Med Assoc. 2020; 70(9): 1648-50. http://doi.org/10.5455/JPMA.46528.
40. Ksiazek S, Grover S, Mojica G et al. Indocyanine green toxicity of the retina after cataract surgery: a case report. Retin Cases Brief Rep. 2009; 3(2): 115-7. http://doi.org/10.1097/ICB.0b013e318162b123.
41. Yeh LK, Yang CS, Lee FL et al. Solar retinopathy: a case report. Zhonghua Yi Xue Za Zhi (Taipei). 1999; 62(12): 886-90.
42. McDonald HR, Harris MJ. Operating microscope-induced retinal phototoxicity during pars plana vitrectomy. Arch Ophthalmol. 1988; 106(4): 521-3. http://doi.org/10.1001/archopht.1988.01060130567038.
43. Witkin AJ, Chang DF, Jumper JM et al. Vancomycin-Associated Hemorrhagic Occlusive Retinal Vasculitis: Clinical Characteristics of 36 Eyes. Ophthalmology. 2017; 124(5): 583-595. http://doi.org/10.1016/j.ophtha.2016.11.042.
44. Hsu ST, Ponugoti A, Deaner JD et al. Update on Retinal Drug Toxicities. Curr Ophthalmol Rep. 2021; 9(4): 168-77. http://doi.org/10.1007/s40135-021-00277-x.
45. Hydroxychloroquine Toxicity. Weng CY, Kim JE, Leng T et al (eds.). EyeWiki, San Francisco 2025.
46. Wang G, Zhuo N, Liao Z et al. Retinal toxicity caused by hydroxychloroquine in patients with systemic lupus erythematosus: A case report. Medicine (Baltimore). 2021; 100(22): e25688. http://doi.org/10.1097/MD.0000000000025688.
47. Ding HJ, Denniston AK, Rao VK et al. Hydroxychloroquine-related retinal toxicity. Rheumatology (Oxford). 2016; 55(6): 957-67. http://doi.org/10.1093/rheumatology/kev357.
48. Pereira C D R, Miguel V S, Miguel TS et al. Early and progressive hydroxychloroquin retinal toxicity: 9-year follow-up with multimodal retinal imaging. Int J Med Ophthalmol. 2022; 4(2): 9-14. http://doi.org/10.33545/26638266.2022.v4.i2a.120.

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