What We Know — And Don't Know — About Blue Light

Evidence-based guidelines for recommending blue light filtration for your patients

TECHNICAL WHITE PAPER

HOYA

In recent years, high-energy visible (HEV) blue light has been one of the most talked-about topics in eye care. Much of this emphasis on blue light has grown from concerns about potential harmful ocular effects of extensive and sustained use of computers and other digital devices that have luminous LED displays.

According to The Vision Council Digital Eyestrain Report (June 2017), 83.6 percent of Americans age 18 and older typically use computers and other digital devices at least 2 hours per day, and 50.3 percent use these devices at least 6 hours per day. Among parents surveyed, 72.9 percent reported that their children spend at least 2 hours per day in front of a digital device screen.[1]

Also, 62.2 percent of survey respondents said they were either "very concerned" or "somewhat concerned" about the impact of digital device usage on their eyes, and 77.1 percent were "very concerned" or "somewhat concerned" about the impact of digital devices on their children's developing eyes.[1]

To address concerns about potential ocular and visual effects from blue light, eyewear manufacturers have introduced an array of eyeglass lenses designed to shield wearers' eyes from HEV blue light radiation.

But how much of this concern about blue light hazard of computers and other digital devices is based on solid research? And what is the most effective way to limit blue light exposure?

In this paper, we will review peer-reviewed published research concerning the interaction of blue light and the eye, and the potential risk(s) blue light poses to the eye and visual system.

Based on this review, we will provide a list of practical, fact-based guidelines for recommending eyewear that provides filtration from HEV blue light radiation.

> **"77.1% were "very concerned" or "somewhat concerned" about the impact of digital devices on their children's developing eyes.[1]**

What is blue light?

Visible light is electromagnetic radiation that can be seen by the human eye and includes wavelengths ranging from 380 to 780 nanometers (nm).

However, there are different standards around the globe and some organizations say the cutoff between invisible UV radiation and high-energy visible light occurs at 400 nm rather than 380 nm. For example, while the American National Standards Institute (ANSI) and the International Organization for Standardization (ISO) consider electromagnetic radiation with wavelengths 380 to 400 nm to be visible light in specific standards, the World Health Organization (WHO) and the Australian Radiation Protection and Nuclear Safety Agency say electromagnetic rays with wavelengths ranging from 380 to 400 nm are invisible UV radiation.[2-5]

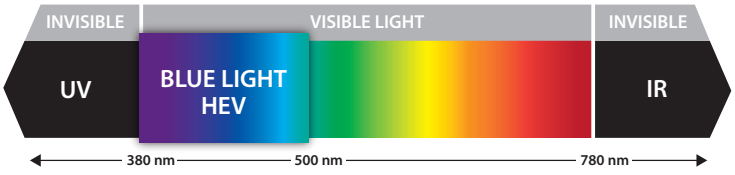
For the purpose of this paper, we will be using the classification of visible light defined by ANSI Standard Z80.3-2015 [Ophthalmics – Nonprescription Sunglass and Fashion Eyewear Requirements] and ISO Standard 8980-3:2013 [Ophthalmic Optics – Uncut Finished Spectacle Lenses – Part 3: Transmittance specifications and test methods], which are widely used in the ophthalmic lens industry and define visible light as beginning at 380 nm.

The energy of specific rays of visible light (and all electromagnetic radiation) is inversely related to wavelength. HEV blue light is at the high-energy end of the visible light spectrum, consisting of light rays with wavelengths ranging from 380 to 500 nm.

In the broad spectrum of electromagnetic radiation, visible light occupies a relatively narrow band, bracketed between invisible ultraviolet (UV) radiation and infrared (IR) radiation.

UV radiation has higher energy than visible light, with wavelengths ranging from 100 to 380 nm. It is further classified as UVC (100-280 nm), UVB (280-315 nm) and UVA (315-380 nm).[2]

Invisible IR radiation has less energy than visible light and consists of wavelengths ranging from 780 nm to approximately 1 millimeter (mm).



HEV – High Energy Visible Light, UV – Ultraviolet Light, IR – Infrared Light

Though discussion of the potential harmful effects of UV and IR radiation on the eye are beyond the scope of this paper, it is established that cumulative exposure to UV rays over the course of years has been associated with an increased risk of cataracts[6-10] and anterior lesions of the eye and surrounding tissues, including pterygia[11-14], ocular melanomas[15] and skin cancer affecting the eyelids.[16]

A confounding factor when evaluating the potential effects of HEV blue light on the eye is that different scientific disciplines and researchers use different definitions of blue light. Specifically, some researchers define HEV blue light as wavelengths ranging from 380 to 500 nm, whereas others may define it as wavelengths within the 400 to 500 nm range.

In this paper, we have attempted to summarize research from a wide range of respected sources to provide practical insight into potential effects of HEV blue light on the eye, acknowledging that researchers may define blue light somewhat differently.

The mechanism behind blue light hazard

When radiant energy is absorbed by a biological tissue such as the eye, this transfer of energy can cause two types of damage to the absorbing tissue: photochemical damage and heat damage. In the case of HEV blue light, the concern primarily is its potential to cause photochemical changes in ocular tissues.

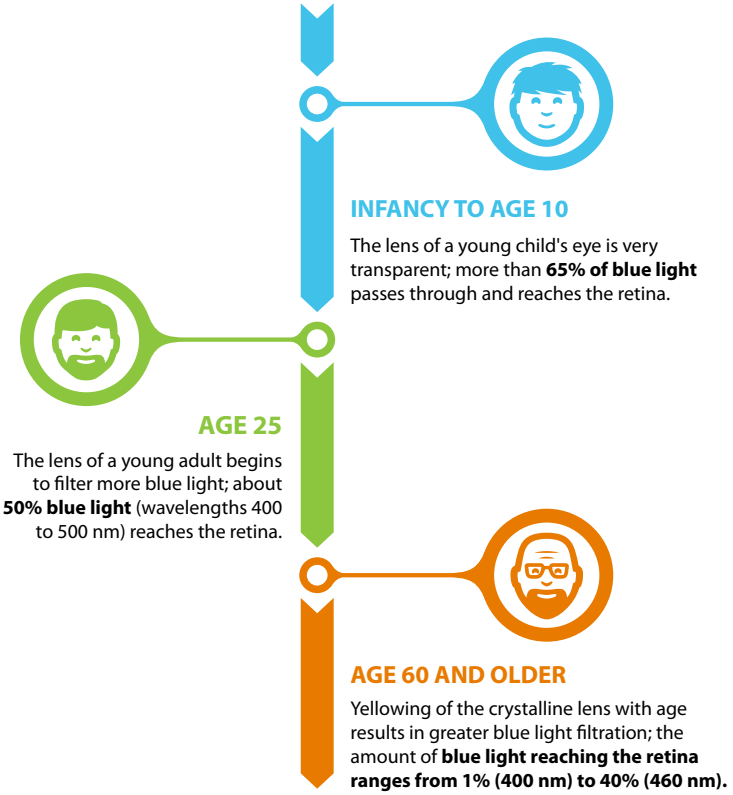
Photochemical damage occurs when HEV blue light is absorbed by molecules in ocular tissues, leading to the formation of excited states of these molecules that can induce chemical transformations within them. These excited molecules also can affect other molecules they interact with, causing them to become chemically reactive as well. This process — leading to the development of free radicals and reactive oxygen species (ROS)[17] — ultimately may lead to structural and functional damage to ocular tissues.

How blue light affects specific ocular tissues

To understand the risks posed by HEV blue light on specific structures of the eye, the first step is to recognize how much radiation at specific wavelengths are absorbed and/or transmitted by ocular tissues.

It's also important to recognize that aging affects how much blue light energy is absorbed by specific tissues — especially changes to the crystalline lens. In other words, the lens of a child's eye will have significantly different absorption/transmittance values compared with those of an older adult, which in turn will influence how much radiant energy reaches the retina.

How Blue Light Absorption Changes With Age

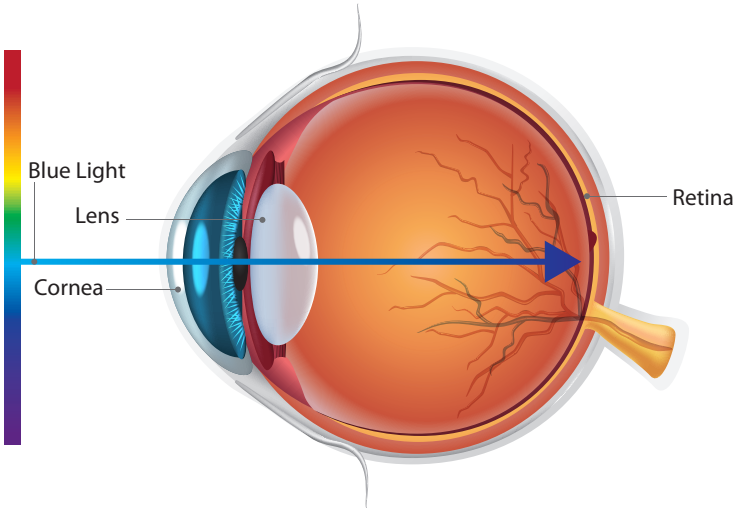


Source: Behar-Cohen F, et al. Light-emitting diodes (LED) for domestic lighting: Any risk for the eye? Progress in Retinal and Eye Research. 2011: 30, 239-257.

Cornea

Virtually all HEV blue light passes through the cornea.

But research has shown that HEV blue light of wavelengths 410 nm and 480 nm emitted by LED lamps can induce oxidative damage to cultures of human corneal epithelial cells, whereas irradiation with visible light of longer wavelengths did not.[22] Because other research has shown oxidative stress and inflammation of the ocular surface play a role in the development of dry eye disease,[23,24] the study authors suggested that interventions that reduce oxidative damage of the cornea induced by blue light "may also be effective in the treatment of oxidative stress-induced ocular surface diseases, including dry eye."[22]



It is important to note, however, that dry eye is a complex condition and more research is needed to better understand the potential role of oxidative stress induced by blue light exposure may play in the development of dry eye disease.

Lens

There are changes in the absorption characteristics of the crystalline lens with age, and these changes primarily affect how much HEV blue light passes through to the retina.

In the eyes of a young child, more than 65 percent of HEV blue light (defined as 400 to 500 nm) passes through to the retina. But by age 25, this amount is reduced to 50 percent of total HEV blue light, 20 percent of the blue light spectrum ranging from 400 to 460 nm, and 50 percent of blue light ranging from 400 to 500 nm.[17]

Yellowing of the lens that occurs with age continues to increase the amount of blue light that is absorbed by the lens. By age 60 to 70, the amount of blue light reaching the retina ranges from 1% (400 nm) to 40% (460 nm).[17]

Though it has been established that cumulative exposure to UVB and UVA radiation is associated with the development of cataracts,[6-8] it's unclear at this time whether HEV blue light is involved in cataract formation.

Retina

Because blue light penetrates all the way to the back of the eye, the greatest ocular hazard from HEV blue light appears to be retinal damage — particularly the macula.

The macular pigment plays an important role in protecting the macula from oxidative stress caused by HEV blue light. This yellow pigment — which consists of the carotenoids lutein, zeaxanthin and meso-zeaxanthin efficiently absorbs blue light between 400 nm and 500 nm.[29-31]

By absorbing blue light, the macular pigment limits the production of reactive oxygen species (ROS), which are induced by HEV light rays. Also, the macular pigment neutralizes existing ROS, thereby further reducing the risk of oxidative injury to the macula.[32,33]

Though it appears macular pigment levels stay relatively constant throughout life,[34] epidemiological studies have revealed that low macular pigment levels are associated with higher risk of age-related macular degeneration (AMD).

The macular pigment also preserves or enhances visual function in a variety of ways. The filtration of blue light reduces chromatic aberration, which can enhance visual acuity and contrast sensitivity. The macular pigment also reduces discomfort glare (photophobia and discomfort experienced when intense light enters the eye) and improves photostress recovery time (the time required for retinal photopigments to regenerate after the eye is exposed to a bright light source), macular function and neural processing speed.[29]

> **"In the eyes of a young child, more than 65% of HEV blue light (defined as 400 to 500 nm) passes through to the retina.**

Though additional research is needed to determine if prolonged exposure to blue light decreases the ability of the macular pigment to protect the eye from AMD and other retinal degenerative changes (and, if so, how it does this), the association between low macular pigment levels and higher risk of AMD suggests it may be prudent to attempt to limit the cumulative levels of blue light reaching the retina over a person's lifetime.

Lipofuscin and blue light hazard

Retinal pigment epithelium (RPE) cells play an important role in the removal of oxidized outer segments of photoreceptor cells in the retina and the regeneration of visual pigments.[17]

RPE cells also contain granules of melanin — a pigment which absorbs excess UV and visible light reaching the retina at wavelengths between 300 to 700 nm.[35]

But as RPE cells age, a substance called lipofuscin accumulates within them. The lipofuscin found in RPE cells is mainly derived from the chemically modified residues of incompletely digested photoreceptor outer segments.[36]

Lipofuscin acts as a photosensitizer — meaning it increases the sensitivity of the retina to damage from light energy. When exposed to high energy visible blue light, lipofuscin induces photochemical changes that can cause permanent damage to the retinal pigment epithelium and photoreceptor cells in the retina.[37,38]

Also, changes in the lipofuscin within RPE cells with age appear to increase its photosensitizing effects.[36] Therefore, lipofuscin in older eyes may induce more oxidative damage to the retina under blue light exposure than in young eyes.[29]

These and other findings have led researchers to conclude that stimulation of lipofuscin within the RPE by high-energy blue light with wavelengths ranging from 400 to 460 nm can cause permanent damage to the retina.[42-44]

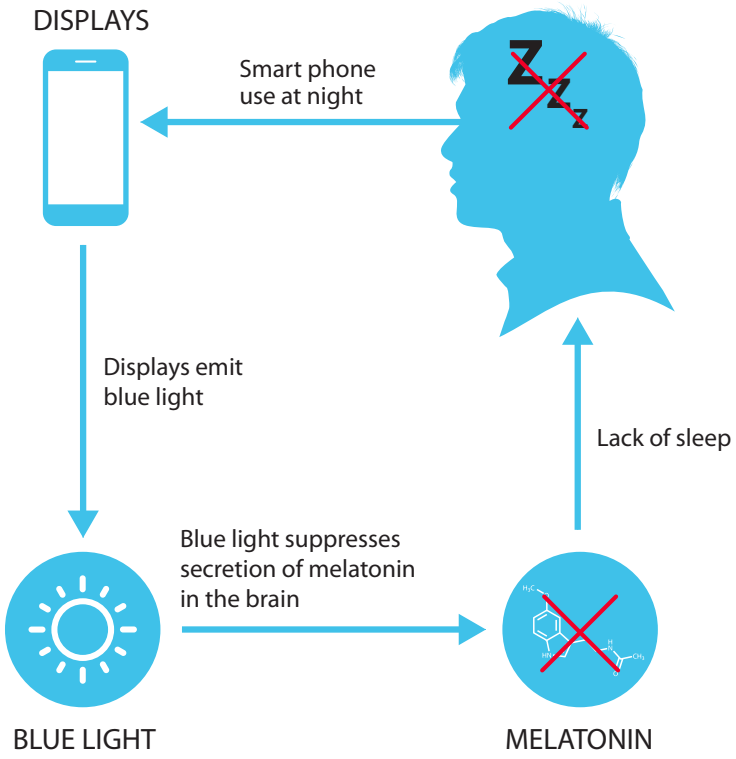
Blue light and circadian rhythm

Circadian rhythm refers to the 24-hour cycle that our bodies and physiological processes undergo on a daily basis, including our sleep cycle.

Though not all details of circadian rhythm are completely understood, this "biological clock" is controlled by a small structure called the suprachiasmatic nucleus (SCN) located in the hypothalamus of the brain. This structure contains nerve cells that influence the release of melatonin — a hormone secreted by the pineal gland that helps bring about and maintain restful sleep.[45]

The SCN requires environmental clues — especially light — to keep our bodies on an accurate 24-hour cycle. Exposure of the retina to longer-wavelength blue light in particular appears to have a significant influence on the SCN and circadian rhythm, reducing the secretion of melatonin and affecting our ability to fall asleep.[46]

This is a potentially serious problem because more and more people these days are being exposed to blue light from electronic devices well into the night. According to The Vision Council Digital Eyestrain Report (June 2017), over 80 percent of adult Americans use digital devices (including television) within an hour of going to bed.[1]



Also, the relatively recent shift from incandescent light bulbs to more energy-efficient LED (light-emitting diode) and CFL (compact fluorescent lamp) bulbs — which emit more blue light than the incandescent bulbs they are replacing — further increases the potential for decreases in melatonin secretion and disruption of circadian rhythm.

Given the newness of this lighting technology shift (now primarily to LED sources), more research will be needed to effectively evaluate the safety of long-term exposure to low levels of blue light. However, some studies already are suggesting that exposure to blue light emitted from LED room lighting and digital devices at the end of the day can have significant effects on alertness before and after sleep.

One study evaluated the effect of three different types of indoor lighting for two hours in the evening on melatonin suppression, alertness and cognitive performance of 16

healthy young men. The researchers found that CFL bulbs with a high color temperature (6500K "daylight equivalent" CFLs) that emit more high-energy blue light produced more melanin suppression and alertness before bedtime than CFL and incandescent light sources with lower color temperatures (2500K and 3000K "soft white" bulbs).[50]

In another study, researchers found that when healthy young adults spent several hours reading an e-book displayed on a digital device before bedtime for five consecutive evenings, it took them longer to fall asleep and they had reduced next-morning alertness, compared with matched controls who spent the same amount of time reading a printed book before bedtime.[51]

In addition to causing daytime drowsiness, lack of adequate sleep (from disruption of circadian rhythm or other causes) has been associated with a greater risk of obesity, diabetes, heart disease and stroke. Also, the American Medical Association has issued a statement saying nighttime lighting is harmful to health and may even increase the risk of certain cancers.[47]

For these reasons, regardless whether eyewear is prescribed to filter HEV blue light, patients should be counseled to turn off their digital devices well before bedtime to reduce the risk of circadian rhythm disruption from blue light.[46]

Primary sources of blue light and relative risk

Generally speaking, the higher the energy (the shorter the wavelength) of visible blue light, the more likely it is to cause oxidative stress that can damage ocular tissues.[17]

But other factors that play a role in the risks to the eye from HEV light ("blue light hazard") are the intensity and duration of the emitted rays.

One measure of light intensity is irradiance, which is defined as the radiant flux (power) of electromagnetic radiation received by a surface per unit area. Irradiance from light sources frequently is measured in units of microwatts per square centimeter ($\mu W/cm^2$).

To keep the relative blue light hazard posed by digital devices in perspective, it's helpful to compare the dose of HEV blue light from these devices to the doses received from sunlight.

When blue light (wavelengths 425 to 465 nm) is measured with a BlueSpec light meter, full sunlight produces irradiance levels up to 1,500 $\mu W/cm^2$. In contrast, a modern LED computer screen at a measuring distance of 24 inches produces blue light irradiance of just 30 $\mu W/cm^2$.

> **"The blue light "dose" from standing outdoors on a sunny day is up to 50 times stronger than that received from a computer screen.**

In other words, the blue light "dose" from standing outdoors on a sunny day is up to 50 times stronger than that received from a computer screen at a normal viewing distance.

Stated another way, in order to sustain the same blue light hazard of spending 15 minutes in full sunlight outdoors, you would need to sit in front of a computer screen for more than 12 hours.[48]

Other sources of blue light

In addition to sunlight, computer screens and other devices with LED displays, the residential and commercial shift from incandescent to LED and other more energy-efficient light sources is another factor in overall blue light exposure.

Though most LED lighting appears white, light emitting diode bulbs have peak emission in the blue light range (400 to 490 nm). Also, white-light LED bulbs degrade over time, causing an increase in color temperature and a corresponding increase in how much blue light is emitted from them.[49]

One thing is certain: People are exposed to significantly more blue light today — from multiple sources — than ever before. Therefore, until the risks of this exposure are fully understood, it's prudent to take reasonable steps to limit blue light exposure when possible.

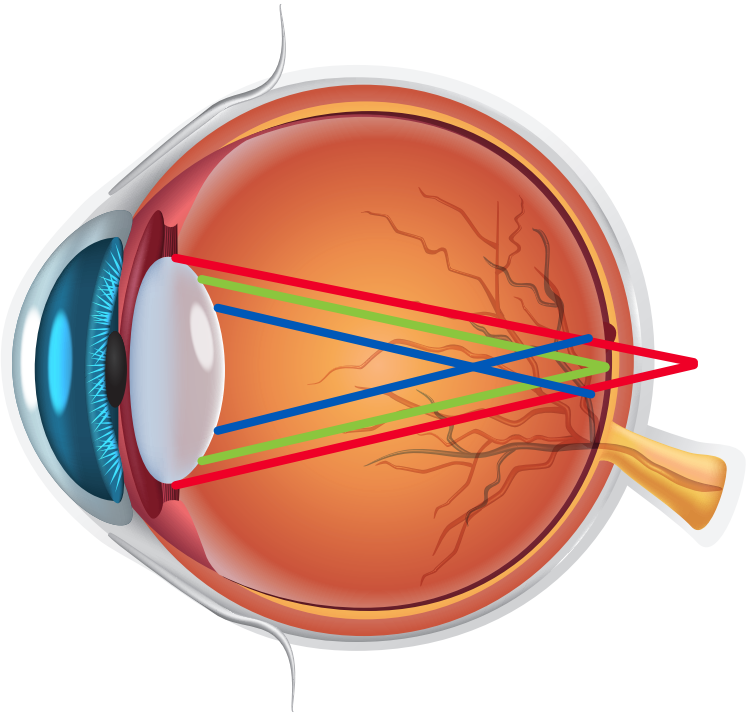
Light scatter and digital eye strain

The Vision Council defines digital eye strain as "physical discomfort after screen use for longer than two hours at a time."[52]

One factor that contributes to digital eye strain is chromatic aberration, which is the production of a defocused color fringe around text or other objects on a digital display.

All eyes have some degree of chromatic aberration, even if vision is corrected as well as possible with prescription eyewear. The human eye is most sensitive to visible light of wavelength 555 nm (green light). When this wavelength is perfectly focused on the retina, HEV blue light is defocused at a point in front of the retina. This can create a violet-blue fringe around objects that can affect visual quality and comfort, and the more blue light entering the eye the more apparent chromatic aberration will be.[53]

CHROMATIC ABERRATION



GREEN LIGHT
in focus on macula

BLUE LIGHT
is defocused at a point in front of the retina

RED LIGHT
is defocused behind the macula

It seems reasonable to conclude that wearing eyeglass lenses that filter blue light may reduce the visibility of this chromatic blur circle, increasing visual comfort and potentially decreasing symptoms of digital eye strain.

Prescribing for blue light filtration: What makes sense?

Currently there are no studies that definitively link blue light exposure with the development of macular degeneration or other serious eye diseases.

However, given the growing body of laboratory research that shows blue light can cause damage to ocular tissues, there is legitimate concern about the potential risks posed by cumulative exposure to the high levels of blue light contained in sunlight.

Also, there is reasonable concern that additional exposure to significant levels of blue light from digital devices — in addition to increasing the risk of eye strain related to chromatic aberration and the potential for circadian rhythm alteration — may pose incremental risks to eye health, and that it may take several decades before we fully understand the seriousness of these risks.

Given these realities and concerns, what strategies should today's eye care practitioners (ECPs) employ to insure they are meeting the current standard of care when prescribing eyeglasses and that their patients are receiving a prudent degree of blue light filtration from their eyewear?

In light of current research on the effects (and potential effects) of blue light on the eye, we feel the following guidelines will enable ECPs to meet or exceed standard of care criteria in the realm of blue light filtration:

1. **Children first.** When prescribing for blue light filtration, think of children first. Given that kids spend significant time in sunlight outdoors and are using digital devices earlier and more extensively than ever before, today's young children will have a greater cumulative lifetime exposure to HEV blue light than their older siblings or their parents. For this reason, and given the current lack of strong clinical evidence regarding potential long-term effects of decades of increased blue light exposure, it seems prudent to recommend blue light filtration for all children. In particular, sunglasses or photochromic lenses should be recommended for outdoor wear to reduce daily HEV blue light exposure from sunlight.

2. **Sunglasses. Sunglasses. SUNGLASSES.** With so much talk these days about the potential risks that digital devices pose to the eyes, it's easy to forget that the sun is BY FAR a more potent source of blue light exposure for most people. Common sense blue light filtration begins with quality sunglasses that significantly reduce the transmittance of HEV blue light. Period.

3. **Consider photochromic lenses.** Prescribing light-sensitive photochromic lenses is the most convenient and affordable way to insure your patients have clear and comfortable vision in all light conditions. Modern photochromic lenses can filter up to twice as much HEV blue light than standard clear plastic or polycarbonate lenses indoors and more than 80 percent blue light outdoors.

4. **High-risk patients.** You also may want to prescribe lenses that filter blue light for patients with a higher-than-normal risk of macular degeneration. These high-risk individuals may include people with a family history of AMD and those who spend long hours outdoors or using computers and other digital devices. People who have undergone cataract surgery also may be more susceptible to blue light hazards, depending on the light-absorptive characteristics of the intraocular lens (IOL) used during their procedure.

5. **Some blue light is beneficial — but not at bedtime.** Blue light in the 460 to 500 nm range is important to the maintenance of a healthy circadian rhythm and accurate color perception during the day. But keep in mind that even this "good" blue light should be limited in the evening to reduce potential disruption of circadian rhythm and sleep disorders. This can be accomplished by turning digital devices off at least 1 to 2 hours before bedtime. Also, choose "soft white" LED light bulbs (color temperature: 2700K) in your bedroom and other living areas to limit the amount of blue light exposure from ambient lighting in your home.

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References

1. The Vision Council Digital Eyestrain Report June 2017. The Vision Council.
2. ANSI Standard Z80.3-2015 [Ophthalmics – Nonprescription Sunglass and Fashion Eyewear Requirements]
3. ISO Standard 8980-3:2013 [Ophthalmic Optics – Uncut Finished Spectacle Lenses – Part 3: Transmittance specifications and test methods]
4. Ultraviolet radiation and health. World Health Organization. http://www.who.int/uv/uv_and_health/en/. Accessed February 2018.
5. Ultraviolet radiation. Australian Radiation Protection and Nuclear Safety Agency. https://www.arpansa.gov.au/understanding-radiation/what-is-radiation/non-ionising-radiation/ultraviolet-radiation. Accessed February 2018.
6. Oliva MS and Taylor H. Ultraviolet radiation and the eye. Int. Ophthalmol. Clin. 2005: 45(1), 1-17.
7. Robman L and Taylor H. External factors in the development of cataract. Eye (Lond). 2005: 10, 1074-1082.
8. Asbell PA, et al. Age-related cataract. Lancet 2005: 12-18(365), 599-609.
9. Hollows F and Moran D. Cataract - the ultraviolet risk factor. Lancet 1981: Dec, 1249-1251.
10. Taylor H, et al. Effect of ultraviolet radiation on cataract formation. New Eng. J. Med. 1988: 319, 1429-1433.
11. Taylor H. Aetiology of climatic droplet keratopathy and pterygium. Br. J. Ophthalmol. 1980: 64, 154-163.
12. Saw S and Tan D. Pterygium: prevalence, demography and risk factors. Ophthalmic Epidemiol. 1999: 6(3), 219-228.
13. Taylor H, et al. The long-term effects of visible light on the eye. Arch. Ophthalmol. 1992: 110(1), 99-104.
14. Moran D and Hollows F. Pterygium and ultraviolet radiation: a positive correlation. Br. J. Ophthalmol. 1984: 68, 343-346.
15. Guenel P, et al. Occupational risk factors, ultraviolet radiation, and ocular melanoma: a case-control study in France. Cancer Causes Control 2001: 12(5), 451-459.
16. Sun EC, Fears TR and Goedert JJ. Epidemiology of squamous cell conjunctival cancer. Cancer Epidemiol. Biomarkers Prev. 1997: 6(2), 73-77.
17. Behar-Cohen F, et al. Light-emitting diodes (LED) for domestic lighting: Any risk for the eye? Prog. Retin. Eye Res. 2011: 30, 239-257.
18. IARC monographs on the evaluation of carcinogenic risks to humans: Volume 55 - solar and ultraviolet radiation. World Health Organization, International Agency for Research on Cancer. 1992.
19. Vajdic CM, et al. Sun exposure predicts risk of ocular melanoma in Australia. Int. J. Cancer. 2002: 101(2), 175-182.
20. Singh AD, et al. Sunlight exposure and pathogenesis of uveal melanoma. Surv. Ophthalmol. 2004: 49(4): 419-428.
21. Hu DN, et al. Role of ocular melanin in ophthalmic physiology and pathology. Photochem. Photobiol. 2008: 84(3), 639-644.
22. Lee JB, et al. Blue light-induced oxidative stress in human corneal epithelial cells: protective effects of ethanol extracts of various medicinal plant mixtures. Invest. Ophthalmol. Vis. Sci. 2014: 55(7), 4119-4127.
23. Uchino Y, et al. Oxidative stress induced inflammation initiates functional decline of tear production. PLoS One. 2012: 7, e45805.
24. Uchino Y, et al. A new mouse model of dry eye disease: oxidative stress affects functional decline in the lacrimal gland. Cornea. 2012: 31(suppl 1), S63-S67.
25. Gaillard ER, et al. Age-related changes in the absorption characteristics of the primate lens. Invest. Ophthalmol. Vis. Sci. 2000: 41(6), 1454-1459.
26. Bron AJ, et al. The ageing lens. Ophthalmologica. 2000: 214(1), 86-104.
27. van de Kraats J and van Norren D. Optical density of the aging ocular media in the visible and the UV. J. Opt. Soc. Am. A Opt. Image Sci. Vis. 2007: 24(7), 1842-1857.
28. Kessel l, et al. Age-related changes in the transmission properties of the human lens and their relevance to circadian entrainment. J. Cataract Refr. Surg. 2010: 36(2), 308-312.
29. Lima VC, et al. Macular pigment in retinal health and disease. Int. J. Retina Vitreous. 2016: 2(19). Published online August 15, 2016.
30. Wooten BR and Hammond BR. Macular pigment: influences on visual acuity and visibility. Prog. Retin. Eye Res. 2002: 21(2), 225-240.

31. Whitehead AJ, et al. Macular pigment: a review of current knowledge. Arch. Ophthalmol. 2006: 124(7), 1038-1045.
32. Sujak A, et al. Lutein and zeaxanthin as protectors of lipid membranes against oxidative damage: the structural aspects. Arch. Biochem. Biophys. 1999: 371, 301-307.
33. Junghans A, Sies H and Stahl W. Macular pigments lutein and zeaxanthin as blue light filters studied in liposomes. Arch. Biochem Biophys. 2001: 391,160-164.
34. Ciulla TA and Hammond BR Jr. Macular pigment density and aging, assessed in the normal elderly and those with cataracts and age-related macular degeneration. Am. J. Ophthalmol. 2004: 138(4), 582-587.
35. Bok D. Processing and transport of retinoids by the retinal pigment epithelium. Eye. 1990: 4, 326-332.
36. Kennedy CJ, Rakoczy PE and Constable IJ. Lipofuscin of the retinal pigment epithelium: A review. Eye (Lond). 1995: 9(Pt 6), 763-771.
37. Boulton M, et al. The photoreactivity of ocular lipofuscin. Photochem. Photobiol. Sci. 2004: 3(8), 759-764.
38. Wang Z, et al. Oxidation of A2E results in the formation of highly reactive aldehydes and ketones. Photochem. Photobiol. 2006: 82(5), 1251-1257.
39. Reszka K, et al. The photochemistry of human retinal lipofuscin as studied by EPR. Photochem. Photobiol. 1995: 62, 1005-1008.
40. Parish CA, et al. Isolation and one-step preparation of A2E and iso-A2E fluorophores from human retinal pigment epithelium. Proc. Natl. Acad. Sci. 1998: 95, 14609-14613.
41. Wu Y, et al. Structural characterization of bisretinoid A2E photocleavage products and implications for age-related macular degeneration. Proc. Nat. Acad. Sci. USA. 2010: 107(16), 7275-7280.
42. Ham WT. Ocular hazards of light sources: review of current knowledge. J. Occup. Med. 1983: 25(2), 101-103.
43. van Norren D and Schellekens P. Blue light hazard in rat. Vis. Res. 1990: 30(10), 1517-1520.
44. Algvere PV, Marshall J and Seregard S. Age-related maculopathy and the impact of blue light hazard. Acta Ophthalmol. Scan. 2006: 84(1), 4-15.
45. Benarroch E. Suprachiasmatic nucleus and melatonin: reciprocal interactions and clinical correlations. Neurology. 2008: 71(8), 594-598.
46. Blue light has a dark side. Harvard Health Letter. December 30, 2017. https://www.health.harvard.edu/staying-healthy/blue-light-has-a-dark-side.
47. AMA House of Delegates 2012 Annual Meeting: Council on Science and Public Health, Report 4.
48. Vision Ease internal measurements; BlueSpec light meter (425-465 nm).
49. Tosini G, Ferguson I and Tsubota K. Effects of blue light on the circadian system and eye physiology. Molecular Vision. 2016: 22, 61-72.
50. Chellappa SL, et al. Non-visual effects of light on melatonin, alertness and cognitive performance: can blue-enriched light keep us alert? PLoS One. 2011: 6(1), e16429.
51. Chang AM, et al. Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next morning alertness. Proc. Natl. Acad. Sci. USA. www.pnas.org/cgi/doi/10.1073/pnas.1418490112. November 26, 2014 (accessed January 3, 2018).
52. Digital eye strain. The Vision Council. https://www.thevisioncouncil.org/content/digital-eye-strain. (Accessed December 15, 2017).
53. Loughman J, et al. Macular pigment and its contribution to visual performance and experience. J. Optom. 2010: 3(2), 74-90.

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