A REVIEW OF MEDICATIONS THAT CAN AFFECT THE CORNEA


Look out for those that can have irreversible ocular effects.

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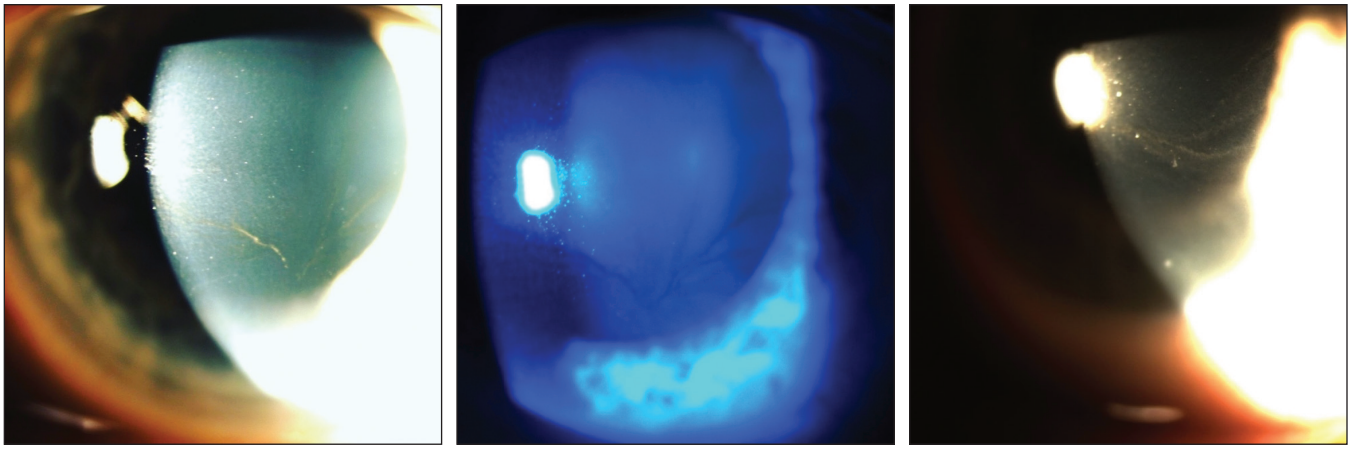
Many medications, both topical and systemic, can affect the cornea. Those that are topically administered have a direct effect on the corneal layers, while those that are systemically administered reach the cornea through the tear film, limbal vasculature, and aqueous humor.[1]

Some drugs can damage the cornea, and drug-induced changes can range from asymptomatic deposits that are incidental findings during an examination to irreversible changes that can be sight-threatening. This article reviews many of the medications seen by ODs when examining patients in clinical practice.

Certain drugs affect a single layer of the cornea, while others affect multiple layers. Examples of medications that affect multiple layers of the cornea are chlorpromazine (a benzodiazepine antipsychotic medication) and rifabutin (an antimycotic antibiotic), which affect both the stromal and endothelial



Images courtesy of Jacob Lang, OD, FAAO

Figure 1. A recognizable sign of corneal verticillata, as shown here, are fine, golden-brown or gray opacities in the basal epithelium that branch out from a central whorl.

layers. Rifabutin causes yellow-brown peripheral deposits that begin in the peripheral cornea and progress to the central cornea.[2] Indomethacin can affect the epithelium and stroma. Suramin can cause vortex keratopathy, epithelial erosions, and punctate keratopathy. Clarithromycin, an antibiotic prescribed for patients with *Mycobacterium avium*, can cause changes in the epithelium and subjective blurred vision, which is typically reversible upon discontinuation of the medication.[3] Topical fluoroquinolones can deposit in the cornea via epithelial defect and corneal ulceration.

EPITHELIUM

There are many medications that cause epithelial changes of the cornea. One of the most familiar conditions seen in optometric practice is vortex keratopathy, also known as corneal verticillata or whorl keratopathy (Figure 1). Other epithelial changes are caused by topical anesthetic abuse or netarsudil. Epithelial changes occur due to accumulation of the medication in the epithelium or from changes in epithelial cell regulation. The migration pattern of epithelial cells is from the limbus to the center of the cornea. Medications such as chloroquine, hydroxychloroquine, and indomethacin can also cause vortex keratopathy. Other NSAIDs, such as ibuprofen and naproxen, can also be culprits. Whorl keratopathy can also be caused by Fabry disease, which is a lysosomal storage disease. It is important to distinguish between Fabry and medication-induced corneal changes due to the systemic ramifications of Fabry disease.

Tamoxifen is a nonsteroidal selective estrogen receptor used for prophylaxis after breast cancer surgery. It can cause subepithelial calcium deposits and photophobia, which are typically resolved by discontinuing the medication. This should be facilitated by the patient's oncologist. Indomethacin can also cause whorl keratopathy and stromal deposits. A number of additional medications, including naproxen, phenothiazines, gold, suramin, and antitumor and antiparasitic agents, can cause vortex keratopathy.[3]

Amiodarone is a medication used to treat atrial fibrillation and ventricular arrhythmias. It can cause various corneal complications, including corneal edema, superficial corneal opacities, and vortex keratopathy, which occurs in 70% to 100% of patients taking this medication.[4] The keratopathy presents as bilateral, golden-brown deposits in a whorl-shaped pattern located in the epithelium. Many patients taking amiodarone will complain of photophobia, foreign body sensation, and halos around lights. Never have a patient

AT A GLANCE

- Many drugs can damage the cornea, and drug-induced changes can range from asymptomatic deposits that are incidental findings during an examination to irreversible changes that can be sight-threatening.
- These medications may interact with the cornea directly or through other outlets, and can affect a single layer or multiple layers, including the epithelium, stroma, and endothelium.
- Cessation of the offending medication or modification of dosage may also provide the patient with an improved clinical course.

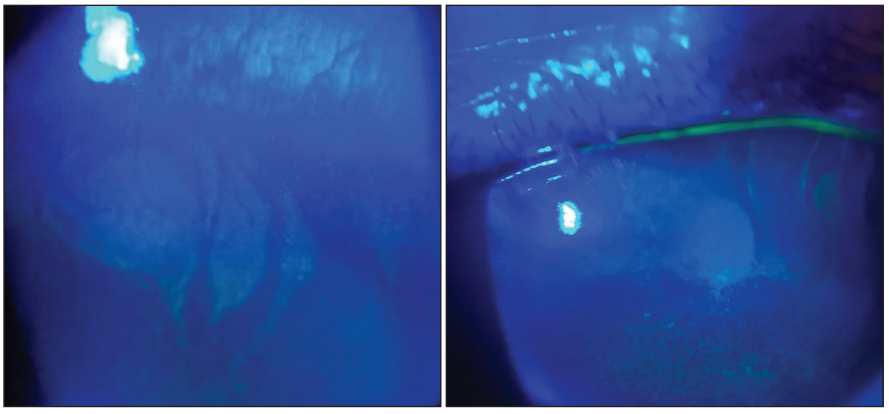


Figure 2. This eye shows the effects of whorl keratopathy.

discontinue amiodarone. Report any ocular effects to the patient's cardiologist or internist.[4]

Graft-versus-host disease is a systemic disorder that occurs following allogenic, hematopoietic stem cell transplantation (Figure 2). The transplanted graft's immune cells recognize the body's host tissues as foreign, causing an overactive inflammatory response that can cause severe ocular surface damage. Bone marrow transplantation effects on the cornea include superficial punctate keratitis, filamentary keratitis, corneal thinning, ulceration, and perforation. Other effects include corneal scarring and neovascularization. An additional finding is limbal stem cell disease. These conditions can be further exacerbated by the harmful effects of radiation and chemotherapy.[5]

Rho kinase inhibitors are commonly used to lower IOP in patients with glaucoma and ocular hypertension. They have the propensity to cause corneal epithelial bullae in a reticular pattern. Additional corneal findings include corneal microcystic edema. The exact etiology of these changes in the epithelium is unclear. Onset of these clinical finds can begin within 1 week of starting this medication. Typically, the epithelial edema resolves within 1 month of discontinuing the medication. Paradoxically, netarsudil is used to reduce corneal edema after endothelial transplantation and Descemet stripping.[6]

STROMA

Numerous medications can cause deposits in the stroma, which may be described as refractile, pigmented, or crystalline.[1] Crystalline deposits can be seen with exogenous immunoglobulin administration. Gold salts used for treatment of rheumatoid arthritis, although not commonly used today, are administered systemically, and can be found in the posterior stroma (aka, ocular chrysiasis).[7] Medications in the phenothiazine family, such as thioridazine and chlorpromazine, which are antipsychotics, can cause pigmentary deposits in the corneal stroma. Tyrosine kinase inhibitor medications, such as vandetanib, which treats leukemia, medullary thyroid cancer, and non-small–cell lung cancer, can also cause stromal deposition, as well as vortex keratopathy. Symptoms of stromal deposition include blurred vision and tearing. Retinoids, such as isotretinoin for acne, can cause fine, diffuse, gray deposits in the superficial stroma in approximately 5% of patients taking this medication. Epithelial thickening and stromal thinning have been reported with the use of isotretinoin.[8]

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"DRUG-INDUCED CORNEAL COMPLICATIONS MAY BE TRANSIENT OR PERMANENT AND MAY HAVE NO EFFECT ON VISUAL ACUITY OR THEY MAY CAUSE MORE SERIOUS SEQUELAE."

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ENDOTHELIUM

As previously mentioned, rifabutin and chlorpromazine can cause refractile deposits in the corneal endothelium by accessing the endothelial cells via the aqueous humor. These deposits, typically gray-white in color, don't usually affect vision. Direct sunlight avoidance helps minimize the photosensitizing effect of these medications. Patients can be referred back to their prescribing physician for dosage modification or drug discontinuation.

A LITTLE KNOWLEDGE GOES A LONG WAY

Drug-induced corneal complications may be transient or permanent and may have no effect on visual acuity or they may cause more serious sequelae. Performing a thorough case history and identifying all current and historic medications will assist in the diagnosis and management of these patients. Careful examination to determine the layer(s) where the pathology is located will also be helpful.

Cessation of the offending medication or modification of the dosage by consulting the appropriate medical personnel in the case of systemic medications may provide the patient with an improved clinical course, provided there are no detrimental effects on the patient's general health or well-being. Topical treatments such as ocular lubricants can offer improved comfort. More involved therapies can be employed for conditions such as limbal stem cell disease and graft-versus-host disease, including topical corticosteroids, autologous serum drops, panretinal photocoagulation drops, amniotic membranes, and scleral lenses, depending on the clinical findings. Importantly, optometrists need to understand the effects of both common and uncommon medications on the cornea. ■

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