

Epithelial Downgrowth

A rare complication returns.

BY SHEILA P. SANDERS, MD

Epithelial downgrowth (ED) is a rare complication of ocular surgery or penetrating ocular trauma that can result in severe secondary glaucoma, among other problems. Several decades ago, ED accounted for up to 27% of enucleations, and it most commonly presented after cataract surgery or ocular trauma, with a surprisingly lower incidence after penetrating keratoplasty, glaucoma surgery, and other procedures.¹ The general consensus holds that the incidence of this complication has declined as surgical techniques and equipment have improved, but few large case series exist. ED still occurs, however, with recent reports in the literature of presentation after Descemet stripping endothelial keratoplasty (DSEK).²⁻⁴ Because early recognition and treatment can greatly improve outcomes, it is important for physicians to consider ED when a patient develops corneal changes or severe glaucoma after ocular surgery or trauma.

THE PERFECT STORM

On average, ED occurs 5 months after surgery or trauma, but the complication can be seen as early as 2 weeks or as late as decades after the initial event.⁵ In most cases, corneal or conjunctival cells migrate into the anterior chamber, but cellular seeding or tissue incarceration could also play a role. Intraocular epithelium does not develop *de novo*; it must gain entry through an opening, usually resulting from inadequate or delayed wound closure, traumatic laceration, or a full-thickness suture tract. An eroded ulcer or implanted device (Figure 1) might also provide access. Healthy migrating endothelial cells will typically close the inner aspect of a wound, providing contact inhibition against any fibrous or epithelial cells that are tracking inward from the ocular surface. Endothelial factors, including incomplete graft attachment, could explain the recent reports in DSEK patients. In addition, DSEK patients often undergo postoperative graft manipulation, requiring the reopening of wounds.

ED has been difficult to reproduce in experimental models. Most epithelial tissue introduced into the anterior chamber will not become established, so clearly, the conditions must be right for it to take hold. Risk factors for ED

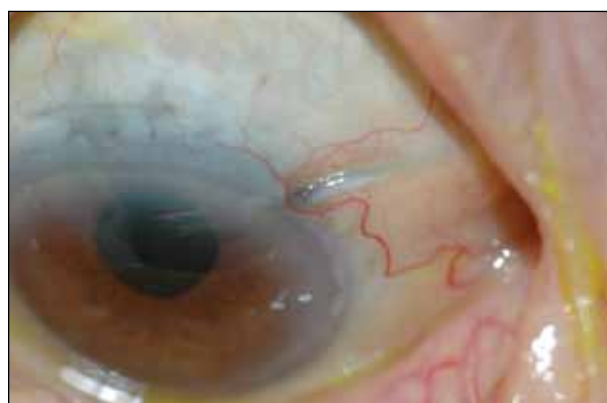


Figure 1. A chronically eroded tube shunt could provide an easy route for epithelial cells to track into the anterior chamber.

include prolonged inflammation and/or corneal vascularization (providing a more nutrient-rich aqueous), stripping of or damage to Descemet layer/corneal endothelium, and hypotony in the setting of a current or previous opening between the chamber and ocular surface.

CHARACTERISTICS—A WOLF IN SHEEP'S CLOTHING

As the multilayered membrane of nonkeratinized, stratified, squamous epithelium (Figure 2) spreads into the eye, it will take on one of three characteristic presentations. "Pearl" or island tumors of the iris are typically small and not aggressive, but they should be excised if they expand. Keratinization has been seen on some of these pearl tumors, which may explain their behavior.⁶

Epithelial cysts are avascular, translucent structures usually arising from the fistulous tract or on the iris. They may expand in size over time.

In the most common sheet form, the epithelial cells spread in a thin layer over all contiguous structures, manifesting as a subtle, gray, translucent membrane that has a smooth border with rolled edges. As the sheet of cells spreads over the angle, it occludes the trabecular meshwork,



(Courtesy of Dr. William R. Morris.)

Figure 2. The advancing sheet of epithelial cells spreads over the angle and anterior iris.

and peripheral synechiae may form, resulting in secondary angle-closure glaucoma. Fibrous or stromal downgrowth, a condition similar to ED that involves the spread of fibrocytes through an ocular fistula, is more common. It presents as a thicker, white, often vascular, retrocorneal membrane with an irregular border. Fibrous downgrowth tissue grows more slowly and carries a somewhat better prognosis.

RECOGNITION AND AGGRESSIVE TREATMENT REQUIRED

Although the early recognition of ED is critical to improving outcomes, the complication can be subtle and difficult to diagnose. Common presentations include glaucoma, corneal edema, hypotony, and the presence of a Seidel-positive opening. Hypotony can suddenly change to a very high IOP when the advancing cells close a chronic fistula.

When ED takes the form of an epithelial cyst, complete excision is recommended. If large, cysts can first be collapsed with needle aspiration. Photocoagulation has been successful for some cysts. Incomplete removal could leave behind cells that will transform into the more aggressive sheet form of ED. When in sheet form, the fine layer of growing cells can be seen spreading circumferentially, then centrally, in from the limbus on the posterior aspect of the cornea. The sheet's leading edge is slightly more defined and is best seen on retroillumination. Iris involvement is similarly difficult to discern, but pupillary distortion and changes in stromal contour may occur. The argon laser can be a useful diagnostic tool: burns made to the involved iris surface will turn fluffy white, whereas normal tissue browns. (Typical settings are 250-350 mJ, 100- μ m spot size, 0.1 seconds.) Laser energy can be applied within 24 hours of a surgical excision for the purpose of localization. Physicians can use fluorophotometry as well as specular and confocal microscopy images

clinically to identify epithelial cells. The diagnosis should be confirmed on histopathological examination. Useful cellular markers, including the sensitive and specific MUC16, have been identified.⁷

The secondary angle-closure glaucoma resulting from ED responds poorly to medical therapy. The goal of treatment is to identify and remove all invading epithelial tissue. Complete resection of involved eye structures, with adjunct cryotherapy to destroy residual cells, is the standard of care. Treatment may require a corneal transplant as well as removal of significant portions of the iris, lens, and vitreous. Despite the collateral damage that can occur with aggressive treatment, it offers a better prognosis than undertreatment or natural progression. Alcohol, 5-fluorouracil, and photocoagulation have also been used in some cases.⁸ Glaucoma shunt surgery is usually required to stabilize the IOP. For palliative treatment, ciliary ablation may be an option. In many cases, it is appropriate to lower patients' expectations: stability and comfort, rather than the complete restoration of visual function, are often a realistic goal. ■

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1. Chen HS, Pineda R. Epithelial and fibrous downgrowth: mechanisms of disease. *Ophthalmol Clin North Am.* 2002;15(1):41-48.
2. Gorovoy MS. Epithelial downgrowth after Descemet stripping automated endothelial keratoplasty. *Cornea.* 2010;29(10):1192-1194.
3. Prasher P, Muftuoglu O, Hsiao ML, et al. Epithelial downgrowth after Descemet stripping automated endothelial keratoplasty. *Cornea.* 2009;28(6):708-711.
4. Walker BM, Hindman H, Ebrahimi K, et al. Epithelial downgrowth following Descemet's-stripping automated endothelial keratoplasty. *Arch Ophthalmol.* 2008;126(2):278-280.
5. Weiner MJ, Trentacoste J, Pon DM. Epithelial downgrowth: a 30-year clinicopathological review. *Br J Ophthalmol.* 1989;73:6-11.
6. Haller JA, Stark WJ, Azab A, et al. Surgical approaches to the management of epithelial cysts. *Trans Am Ophthalmol Soc.* 2002;100:79-84.
7. Vicky C, Pai MD, Glasgow BJ. MUC16 as a sensitive and specific marker for epithelial downgrowth. *Arch Ophthalmol.* 2012;128(11):1407-1412.
8. Shaikh AA, Damji KF, Mintsoulis G, et al. Bilateral epithelial downgrowth managed in one eye with intraocular 5-fluorouracil. *Arch Ophthalmol.* 2002;120(10):1396-1398.

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1. Have you ever personally encountered a case of epithelial downgrowth?

- ☐ Yes
☐ No