

CORNEA

A Post-DSAEK Danger: Epithelial Downgrowth

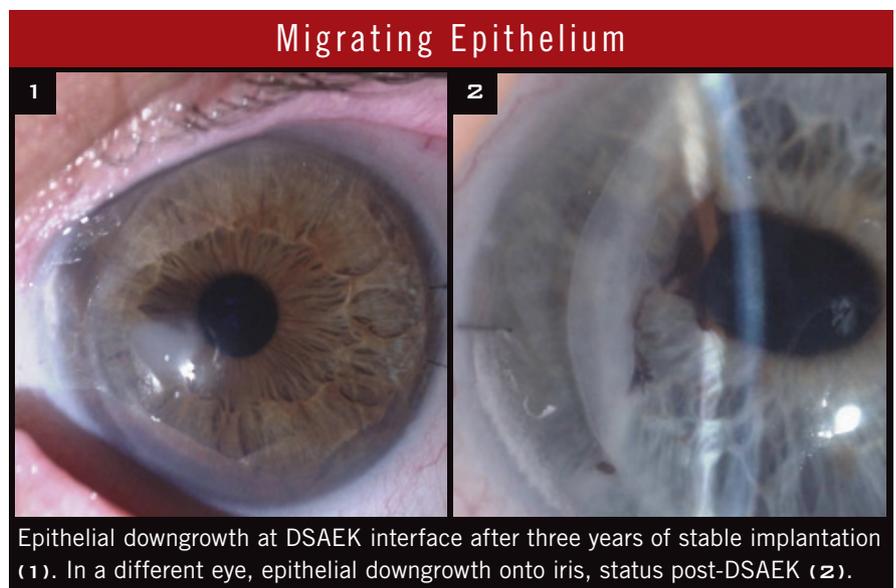
BY MARIANNE DORAN, CONTRIBUTING WRITER

Some corneal transplant surgeons are reporting sporadic cases of epithelial downgrowth after Descemet's stripping automated endothelial keratoplasty (DSAEK). This sight-threatening complication occurs in less than 1 percent of older penetrating keratoplasties, and it is not yet clear whether the incidence will be similar with the newer transplant procedure.

Who's at Risk?

Robert F. Haverly, MD, a cornea surgeon in Erie, Penn., noted that risk factors for epithelial downgrowth include trauma, poor wound healing, multiple surgeries and anterior basement membrane disease. DSAEK maneuvers also increase the risk of downgrowth. These include multiple incisions (especially venting incisions), instruments being taken in and out of the eye while the graft is being positioned, refloating a dislocated or nonadherent graft, and the manipulation involved in releasing the air after surgery.

Unique to DSAEK is the introduction of the donor tissue into the anterior chamber. Despite preventive measures, the donor tissue may have residual epithelial cells attached to it. "You also lose the protective effect of an intact corneal endothelium, which normally inhibits epithelial migration into the eye through contact inhibition," Dr. Haverly said. "DSAEK removes large areas of Descemet's membrane and endothelium, which can leave areas of bare stroma." He



Epithelial downgrowth at DSAEK interface after three years of stable implantation (1). In a different eye, epithelial downgrowth onto iris, status post-DSAEK (2).

noted that prolonged inflammation, hypotony, a vascularized cornea, prolonged graft detachment or incomplete reattachment during DSAEK also can lead to damaged endothelium.

The cells exploit any opening.

Mark S. Gorovoy, MD, a cornea surgeon in private practice in Fort Myers, Fla., said, "In the old penetrating keratoplasty, full-thickness sutures could induce epithelial downgrowth by providing a track where epithelial cells could grow along the suture line and into the anterior chamber. Any track is a conduit for epithelial cells to proliferate and grow down."

Whose Epithelial Cells Are These?

Transplant-related epithelial downgrowth poses an interesting question: Are the proliferating cells from

the patient or the donor? The answer may have a significant impact on a patient's prognosis. "This is a question I've always had in cases of epithelial downgrowth," Dr. Gorovoy said. "There is now a case in the literature in which epithelial cells in the interface were from the donor, appearing to be benign pockets of cells, similar to what may be seen in LASIK.¹ I just submitted a case in which donor cells were growing along the iris, not just on the interface. My case involved epithelial downgrowth into the anterior chamber along the endothelium and iris. This usually forebodes devastating consequences, but my patient has done quite well," Dr. Gorovoy said. "X-Y analysis proved that the cells were from the donor, and they behaved much more benignly than cells that

originate in the recipient. My theory is that because these are foreign cells, the body keeps them in check, almost as if it were trying to reject the cells.”

What to Look For

Dr. Haverly noted that epithelial downgrowth can appear as early as a few days after full-thickness corneal transplant or as long as 10 years later. The problem typically arises six to 11 months after the procedure. One of Dr. Haverly’s patients developed downgrowth eight months after DSAEK. The patient had undergone multiple surgeries, had Fuchs’ dystrophy and required rebubbling of the graft.

Pupils, pressure and graft nonadherence. Early indications of possible epithelial downgrowth include an unexplained increase in intraocular pressure and pupillary distortion. “The pupil can be slightly irregular from the epithelial cells adhering to it or from the iris adhering to the DSAEK graft,” Dr. Haverly said. “Graft nonadherence in the primary surgery and detection of cells in the anterior chamber are other possible signs.”

Reflections. Dr. Gorovoy noted that epithelial downgrowth in the interface is similar to what may be seen with LASIK. “You see these little reflections, which eventually become like small white opacities and in my experience they tend to be isolated islands that generally become arrested and don’t do very much.”

Translucence. In general, tissue growth inside the cornea on the endothelium is manifested as a fine growth that looks like a translucent membrane, Dr. Gorovoy said. “You can see this membrane growing on the iris, where it can cause synechiae and iris distortion as the membrane contracts. The membrane will grow along the endothelium and cause some overlying corneal swelling or edema and some isolated iritis.”

The paracentesis. Dr. Haverly recommended checking the paracentesis site because iris tissue may become trapped there. It can be difficult to see and often does not cause pupillary distortion because it is so peripheral. He

added that any vitreous loss or vitreous wick to the wound should be tested for Seidel positivity.

Beware of mimics. A chronic interface infection can mimic epithelial downgrowth and may not become obvious for some time. Pathological examination of the tissue is important because it may detect microorganisms that have a clinical presentation similar to that of epithelial downgrowth, such as poor vision and low-grade chronic inflammation.

Test modalities. Several tests can help confirm the presence of epithelial downgrowth, including biomicroscopy, spectral microscopy and confocal microscopy. “Laser photocoagulation with an argon laser can mark the edges of the downgrowth because it causes a fluffy whitening of the epithelial membrane, which is not seen in a normal iris stroma,” Dr. Haverly said. “But it’s very difficult to determine the extent of the downgrowth because it may be in the angle or other areas where it would be difficult to detect. Many times, following the blood vessels can lead you to where the epithelial cells are coming from.”

Treating Downgrowth

When epithelial downgrowth involves an isolated membrane in only one area of the eye, several treatment options are available—although none is ideal. The options include cryotherapy, surgery and laser treatment. A cyst can be drained and injected with 5-fluorouracil (5-FU). Treatment usually needs to be repeated more than once.

Early treatment. Dr. Haverly noted that when epithelial downgrowth is discovered early, radiation therapy, surgical scraping, peeling, alcohol treatment and wide excision are treatment possibilities. A conservative approach is to close a wound that is Seidel positive and apply cryotherapy to the stem cells that are producing the epithelial cells entering the eye.

“You can also aspirate a cystic area,” Dr. Haverly said. “Some surgeons use gonioscopy to confirm the anatomy and guide the needle through the limbus and into the cyst. The anterior

chamber is filled with air to protect the other intraocular contents and structures while the cryotherapy is performed.” Photocoagulation has also been tried.

Later treatment. In cases where the epithelial cells have spread and cannot be removed, 5-FU is an option, said Dr. Haverly. “You can do a pars plana vitrectomy with air/fluid exchange. The pupil is constricted with Miostat, and the 5-FU is then injected into the anterior chamber. The posterior segment remains filled with air. Postoperatively, the patient keeps his or her head down to allow the 5-FU to accumulate in the area of the epithelial downgrowth. This may be a good option when the epithelial downgrowth is diffuse.” Dr. Haverly noted that 5-FU is toxic to the eye at certain concentrations, but can be well tolerated when administered correctly.²

When primary treatment is too late. “The goal is to catch epithelial downgrowth early and, if it’s localized, remove it,” Dr. Gorovoy said. “But that tends not to be the case because it usually isn’t recognized early. If the epithelial downgrowth is in the anterior chamber, severe secondary glaucoma is almost guaranteed. This will require shunt surgery. Once it gets to that stage, unless you do aggressive surgery to remove the downgrowth, you are not going to get it all. And then your goal is purely comfort. You treat the glaucoma but don’t keep performing heroic transplants because the cornea will continue to fail due to epithelial regrowth on the endothelial side.”

Act with conviction. “Early treatment is definitely better than late treatment in a more aggressive form, and it decreases the need for enucleation,” Dr. Haverly said. “I think it’s best to always treat epithelial downgrowth aggressively. In my opinion, you only have one shot, and you might as well go in with both barrels blazing. There is just too much at stake not to.”

1 Prasher, P. et al. *Cornea* 2009;28(6):708–711.

2 Shaikh, A. A. et al. *Arch Ophthalmol* 2002;120(10):1396–1398.