Complications of Laser in situ Keratomileusis: Etiology, Prevention, and Treatment

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ABSTRACT

PURPOSE: To review the etiology, prevention, and management of laser in situ keratomileusis (LASIK) complications.

METHODS: Review of literature and the experience of the authors.

RESULTS: Careful preoperative screening is critical to prevention of many potential complications of LASIK. Flap complications that occur during surgery are typically managed by replacement of the flap and repeating the surgery or applying special methods such as transepithelial photorefractive keratectomy weeks to months following the initial procedure. A common source of serious complications is the use of a microkeratome that functions after improper assembly. Timely treatment of postoperative complications such as diffuse lamellar keratitis, flap striae, and infection is critical to an optimal outcome.

CONCLUSION: Most complications of LASIK can be treated effectively and have minimal effect on the final outcome after surgery, if appropriate methods are used for management. [J Refract Surg 2001;17:350-379]

PREOPERATIVE MEASURES TO REDUCE COMPLICATIONS

Many laser in situ keratomileusis (LASIK) complications can be avoided through careful patient screening and preparation for surgery. The first step in preparing a patient should be assessment of expectations. The staff and surgeon must educate the patients while striving to understand the motivation for seeking refractive correction. The simple question, “Why are you considering refractive surgery?” will often reveal a misconception about what LASIK can achieve. For example, patients with presbyopia will often respond that they want to be able to see distance and near without ever needing glasses. Patients with amblyopia will commonly respond that they are hoping the procedure will restore their vision. Many patients will assert that they want to “see 20/20 without ever wearing glasses again.” These types of misconceptions need to be identified and the expectations brought in line with what is achievable. The staff and the surgeon need to accept that there will always be patients who simply will not understand the limitations of surgery. An example is the patient who, despite counseling about the reality of LASIK, repeatedly asks, “So I’m going to be 20/20 after LASIK, right?” Do not hesitate to tell such a patient that they are not a candidate for the procedure. Careful screening will help the surgeon and staff avoid hours of wasted time dealing with a disappointed patient and reduce exposure to litigation.

Each surgeon should understand the limits of LASIK and avoid extending the procedure beyond these limits, where the efficacy and safety of the procedure is compromised. Ultimately the surgeon must decide for himself or herself what limits will be based on: important patient factors such as refractive error, corneal curvature, and corneal thickness, as well as the limitations of the specific laser and technique. For example, we never attempt correction beyond +5.00 diopters (D) of hyperopia or -12.00 D of myopia corrected to the corneal plane because of increased risk of reduced vision quality. However, in some eyes even these limits are excessive depending on the preoperative corneal curvature or corneal thickness. The concept of establishing limits and sticking to them is critical to the safe and effective application of LASIK.

Candidates for LASIK should have a stable refraction, normal corneal topography, and corneas that are free of diseases that predispose to complications. Refractions may be unstable due to
progressive myopia, cataract, corneal ectasia, or other factors. LASIK can still be an appropriate treatment for a patient with progressive myopia, as long as the patient understands and accepts that although a high proportion of the myopia can be corrected, there is a high likelihood of return of myopia over time. Many of these patients happily accept the prospect of having mild to moderate myopia, if their high myopia can be markedly reduced.

There are several important points regarding contact lens management. 1) Corneas must have normal and stable corneal topographic patterns prior to surgery or there will be avoidable errors introduced into the correction and the potential for permanent introduction of irregular astigmatism as a result of the superimposed laser ablation. There is no hard evidence that this can happen, but it seems reasonable to consider this likely. 2) If a patient has contact lens warpage, there is no way to determine how long the contact lenses must be removed to allow the warpage to resolve. 3) Warpage with gas-permeable or hard contact lenses that is superior riding often simulates keratoconus (Fig 1A). Our typical protocol is to remove soft contact lenses for 3 days and rigid contact lenses for 3 weeks prior to the preoperative examination. These time frames will allow warpage to resolve in the majority of patients, based on our prior studies. If warpage is still present at the preoperative examination, the patient is followed at 2- to 4-week intervals until corneal topography becomes normal and stable. In rare cases, such warpage may take 6 to 12 months to resolve. Occasionally a patient with permanent warpage will be detected. If significant irregular astigmatism is present, LASIK is probably contraindicated.

Keratoconus is another disorder that needs to be detected prior to refractive surgery (Fig. 1B). Some surgeons have used photorefractive keratectomy (PRK) or LASIK to treat myopia associated with mild to moderate keratoconus. Although results have been acceptable with relatively short follow-up, much longer observation is necessary to support a stromal thinning procedure for treatment of a
disease that is characterized by progressive stromal thinning over a period measured in decades. Serious complications have been reported. Keratoconus has been associated with chronic keratocyte apoptosis and LASIK or PRK can trigger high levels of keratocyte apoptosis associated with the surgery. Although direct evidence is lacking, it seems plausible that the triggering of accelerated keratocyte apoptosis could be associated with an accelerated disease process. At the least, the patient should be advised of the potential complications associated with application of LASIK to a cornea that has true keratoconus.

Although most surgeons exclude patients with frank keratoconus from consideration from LASIK, the most common difficulty arises in distinguishing early keratoconus from a normal relatively asymmetric astigmatism pattern (Fig 1C). Corneal thickness measurements can be helpful. Corneas with measurements thinner than 500 µm more likely represent true keratoconus. However, even this is not diagnostic because many patients are seen with completely normal corneal topography and corneal thickness less than 500 µm. Thus, some of these patients may be normal with asymmetric astigmatism. If there is concern that a particular patient has early keratoconus, based on the topographic pattern and corneal thickness, then the best course is to delay consideration for 1 or 2 years, with monitoring. Automated indices are available to help with detection of keratoconus.

True keratoconus is characterized by progression. Unfortunately, relatively quiescent periods and progressive periods also characterize true keratoconus. Thus, it is possible that the period of observation coincides with a period of quiescence in an individual patient. Despite the best of intentions, surgeons will be likely to operate on some patients who have true keratoconus unless all patients with keratoconus-like topographic patterns are excluded. Ultimately, each surgeon must decide how to manage these patients.

Epithelial basement membrane degeneration is another disorder that should, when possible, be detected prior to LASIK (Fig 2). The presence of this disorder predisposes to flap complications and irregular healing associated with epithelial sloughing at the time of flap formation. The typical map-dot-fingerprint opacities in the epithelium should lead the surgeon to be wary of performing LASIK. Patients with mild to moderate myopia or hyperopia may be best treated with PRK. It is clear that there are patients with poor epithelial adhesion typical of epithelial basement membrane degeneration with no map-dot-fingerprint opacities in the epithelium. These patients are currently undetectable and the first sign of the problem is typically a large epithelial slough at the time of LASIK surgery in the first eye. Many of these patients do well despite slower visual recovery after surgery if a bandage contact lens is worn for several days to a week following the procedure. This is not always the case, however, and some of these patients develop regression, diffuse interface keratitis, and other complications. If a significant slough is noted in the first eye, there is high risk of a similar occurrence in the second eye and
consideration should be given to changing to PRK in the second eye.

Dry eye is a challenging and potentially serious problem in LASIK patients. Many patients who present seeking LASIK have mild to moderate dry eye and resulting contact lens intolerance. Many of these patients undergo LASIK and have uneventful courses with excellent results. Complications such as abnormal wound healing seem more likely to occur in patients with severe dry eyes.

There is another associated problem that we refer to as LASIK-induced neurotrophic epitheliopathy. LASIK-induced neurotrophic epitheliopathy is attributable to interruption of sensory nerve input to the epithelium of the LASIK flap. This results in a transient abnormality of the flap epithelium associated with punctate epithelial erosions and rose bengal staining. This condition occurs in 1% to 2% of eyes with no evidence of pre-existing dry eye. However, our impression is that it is more common and more severe in patients who have pre-existing dry eye disease. The patients who develop severe LASIK-induced neurotrophic epitheliopathy may have marked visual disability due to epithelial abnormalities overlying the pupil that may last for 6 months or longer. Because of concerns about healing and development of severe LASIK-induced neurotrophic epitheliopathy, we consider any patient with more than mild corneal rose bengal staining or a Schirmer test without anesthesia less than 2 mm in 5 minutes not to be a candidate for LASIK. Even patients with less severe signs of dry eye may be better candidates for PRK, since a condition like this is rare following this surface procedure that ablates only the corneal sensory nerve endings.

Patients with autoimmune disorders occasionally seek LASIK. Surgeons are rightfully concerned that the patient could develop chronic keratitis or corneal melting syndrome. Our general rule is to not offer refractive surgery to any patient with ocular manifestations of autoimmune disease or one who is on systemic medications for autoimmune disease. We have operated on patients with vague histories of autoimmune disorders that have little in the way of symptoms and signs of disease without encountering problems after LASIK. If we have concerns, we ask the patient to have a rheumatologic evaluation to determine whether there is active disease. If we are concerned that the patient may have active autoimmune disease, we do not proceed with surgery.

The effect of keloids frequently arises in a busy refractive surgery practice. Previous studies demonstrated that keloids were not associated with increased complications in PRK. Following this lead, we have performed LASIK on more than 20 patients with a history of keloids without any scarring or other related complications. For the most part, keloids do not appear to be a significant concern for patients considering LASIK.

The question of whether to perform LASIK in a patient with glaucoma is frequently raised due to concern about a reduction in the measured intraocular pressure following surgery and the potential for iatrogenic nerve damage. To our knowledge, there has been only a single report of a nerve defect that may have been attributable directly to LASIK. Since this was only a single case, it is impossible to ascertain whether this was truly associated with LASIK or a mere coincidence in a patient with a family history of glaucoma. We believe it is better to advise against LASIK in patients with severe glaucoma. We consider performing LASIK in patients who are glaucoma suspects, patients who have mild glaucoma, and patients who have moderate well-controlled glaucoma. We advise the patient that a new baseline for intraocular pressure will need to be established by their glaucoma specialist. We also let them know that there is no way at present to be sure there is no risk. We also discuss PRK as an option in patients with low to moderate myopia. Ultimately, we allow the informed patient to make the decision in consultation with the ophthalmologist who treats the glaucoma. There are other less common situations that arise in which the surgeon must make a decision about whether LASIK should be considered. In general, the surgeon needs to use common sense in determining whether a particular patient should have LASIK. When there is significant doubt, the best course of action is typically not to proceed.

INTRAOPERATIVE COMPLICATIONS

An optimal laser room environment is critical for good laser performance. The laser needs to be set up and tested per the manufacturer’s recommendations. The temperature should be maintained between 18° and 24° C and the humidity should be kept at a stable level within the range recommended by the manufacturer. The key is consistency. An environmental control system that maintains constant temperature and humidity and a LASIK nomogram established at those settings may be an important factor in the accuracy and precision of correction in LASIK. Air filtration units are recommended to maintain a clean atmosphere and promote standard laser ablation rates.
Proper assembly of the microkeratome is critical. There is disagreement about whether the surgeon or a technician should assemble the instrument. It has been our practice, for a number of years, to have a well-trained and experienced technician assemble the microkeratome. No complications attributable to this have been noted. If an expert technician is not available, the surgeon should perform the assembly. It is important that the surgeon test run the microkeratome just before it is placed on an eye to make sure it is functioning normally.

The excimer laser should be checked for optimal beam profile, alignment, and other parameters according to the manufacturer’s recommendation. Improper fluence can result in an undercorrection or overcorrection. Poor beam homogeneity can cause an irregular ablation such as a central island or peninsula. Consistency is key. Establish protocols with your staff in consultation with instrument manufacturers and do not depart from them. Do not hesitate to cancel a full day of surgery if a critical instrument is not functioning perfectly.

There are a number of different intraoperative complications (Table) that deserve special discussion. These complications will be covered in following sections.

### Anesthesia and Marking for Cyclotorsion

Topical anesthesia is preferred because it is simple, efficacious, and avoids complications related to retrobulbar and peribulbar infiltration. In addition, these latter methods are associated with poor fixation by the patient on the laser LED target. Mild sedation with oral diazepam (5 or 10 mg) can be considered, but in our opinion, it is rarely necessary.

Topical anesthesia should be used sparingly and should be carefully dosed. Usually two applications just as the procedure begins are sufficient. A toxic effect on the corneal epithelium can result from excessive topical anesthetic. This will exacerbate epithelial adhesion problems that may be noted in patients with occult epithelial adhesion disorders and patients with diabetes mellitus.

A mistake that is frequently made is application of anesthetic to both eyes prior to beginning a bilateral case. Topical anesthetics break down corneal epithelial barrier function. Thus, if the second eye also receives topical anesthetic prior to beginning surgery on the first eye, a minimum of 7 to 10 minutes of exposure will occur prior to surgery in the second eye. During this time interval, corneal hydration will be altered, with unpredictable effects on the nomogram and the accuracy and precision in the second eye. Thus, the carefully established LASIK nomogram will be altered. We recommend applying anesthetic in the second eye just prior to beginning surgery in that eye.

Infiltrative anesthesia may be considered rarely for producing good exposure of sunken eyes or in eyes with narrow interpalpebral fissures. Lateral canthotomy is a better alternative for dealing with deep-set eyes or narrow palpebral fissures because fixation is maintained. Our experience with the Automated Corneal Shapper (Chiron, ACS, Emeryville, CA) and the Hansatome (Bausch and Lomb, Rochester, NY) microkeratomes indicates that this is rarely necessary, even in Asian eyes.

It is our opinion that general anesthesia should not be used for LASIK. Proper centration is currently not possible without the cooperation of the patient fixing on the LED target. This is the case even with lasers that use a tracking system.
A reference mark should be placed with a gentian violet pen or other suitable marker while the patient is in the seated, head erect position so that cyclotorsion that occurs when the patient lies down can be detected. Unless a mark is placed for reference, astigmatic correction could be improperly placed, resulting in undercorrection of astigmatism or even introduction of astigmatism at a different axis. Some surgeons prefer to place these reference marks at the 3 and 9 o'clock positions. Others prefer the 6 o'clock position. It doesn't matter where the mark is made as long as the reticle of the laser can be aligned with it.

Some surgeons do not mark for astigmatism. In the majority of patients, this likely results in minimal, if any, error. However, we have noted cyclotorsion in excess of 20° in some eyes. Induced astigmatism is likely to be generated when this degree of cyclotorsion is present.

Periocular Cleaning and Draping
The eye should be prepared for LASIK as though it were going to be an intraocular procedure. Patients should be instructed not to wear make-up on the day of surgery or for at least 4 days afterward because of the risk of introducing infectious material beneath the flap or into the eye prior to complete healing of the epithelium.

We prefer to prep the eyelids with Betadine swabs such that the lashes and surrounding area are fully treated. Any Betadine that gets into the eye should be removed since the toxicity of this solution could be one cause of diffuse interface keratitis. Removal of the Betadine is facilitated by use of an aspirating lid speculum. Our practice is to apply the first dose of anesthetic prior to the Betadine scrub and the second dose after the scrub, so that any Betadine that gets into the eye is diluted and removed by the aspirating lid speculum. We do not recommend topical antibiotics prior to surgery since no data suggest this decreases the incidence of postoperative infection, and infections are rare.

Some type of sterile drape that effectively captures the lashes should be used. A convenient product that we prefer is a simple oval Tagaderm drape 1624W from 3M (Minneapolis, MN), cut in half. One-half of the drape is applied to the lower lid and one-half to the upper lid. An advantage of this drape is that it will re-stick after removal if it is initially placed improperly. There are many other drapes that are effective and individual surgeons should find one they feel comfortable with and use it consistently. Also, the controls on the excimer laser should be draped; these controls are a source of iatrogenic infection.

The use of sterile gloves by the surgeon is recommended. There are many excellent LASIK surgeons who do not use sterile gloves. However, it is clear that even repeated washing with Betadine or another surgical antiseptic does not eliminate the flora that reside on the hands and beneath the nails. It would be hard to justify not having used gloves in the event of infection.

Exposure of the Eye
Attention to adequate exposure is a critical step in avoiding LASIK complications. Deep orbits, previous orbital fractures, prominent foreheads, small eyes, and narrow palpebral fissures should alert the surgeon to possible intraoperative problems. The surgeon should discuss steps that might be necessary in advance with the patient, including lateral canthotomy, converting to PRK, or abandoning surgery.

We prefer a modified wire speculum with aspiration (Fig 3). There are, however, many specific models of lid specula that are adequate. The key is good, secure retraction of the lids with excellent exposure. Once the lid speculum is in position, the patient's head can be positioned with the neck flexed or extended, depending on the individual patient, to center the cornea in the palpebral fissure.

Many micokeratomes, such as the Hansatome, the Automated Corneal Shaper, and the Innovatome (Inovative Optics, Albuquerque, NM) can be used without a lid speculum because the suction ring itself acts as the lid speculum. This is useful for eyes with a small palpebral fissure to avoid a lateral canthotomy. We recommend that only experienced LASIK surgeons attempt this maneuver.
Inadequate Suction and Intraocular Pressure

The suction ring serves two major purposes: it provides a stable platform to control passage of the microkeratome head. It also hardens the globe to provide depth control during the microkeratome pass. If the globe is too soft, the blade cannot engage the tissue properly. This may result in a thin flap, donut-shaped flap, or free cap. When a buttonhole flap is created, the blade has broken through the epithelium to the surface in the center of the cornea and then returned back into the stroma. A thin or buttonhole flap may also be created if the cornea is steeper than 48.00 D prior to surgery. A cap may also be created when suction is low and is more likely with corneas that are relatively flat prior to surgery.

In rare cases, the thin microkeratome cut does not extend all the way through the epithelium, but actually passes through the layers of the epithelium tangent to the surface. The flap will not have a hole in the center, but there will be a shiny area produced by the epithelial layers adherent to the stroma in the center of the bed beneath the flap. If this is noted, the flap should be replaced without ablation. If this epithelium is scraped away, the bed will be irregular in shape and the refractive outcome will be unpredictable. Similarly, if the ablation is performed over this island of epithelial tissue, a central island will be produced.

All irregular flaps should be returned to their original position without laser treatment. This will be facilitated if the surface of the cornea was marked for orientation prior to beginning the procedure. In most cases, surgery can be repeated after approximately 3 months, with excellent results. In some situations, alternative treatment is needed (discussion follows).

If suction is broken during passage of the microkeratome, the blade will tend to surface. If this occurs, an irregular flap or cap with a cut through the central cornea may result. This potentially serious complication may be reduced by more modern instruments such as the Bausch and Lomb Hansatome that automatically stops if suction is broken during passage of the microkeratome head. However, this type of complication may still occur despite these safety features. The cap or flap should be replaced in its original position. In some cases, the cornea will heal with surprising clarity and consideration can be given to repeating the procedure later. In other eyes, scarring may occur and necessitate other approaches, such as transepithelial phototherapeutic keratectomy, with or without PRK.

The best treatment for inadequate suction is prevention. We prefer to use a pneumotonometer (Mentor Ophthalmics, Santa Barbara, CA, or Solan, Jacksonville, FL) to insure that the intraocular pressure is greater than 75 mmHg when the microkeratome head is placed in position. Other surgeons think the Barraquer tonometer (Bausch & Lomb, Rochester, NY) is adequate.

When suction is inadequate the suction ring should be examined to insure that debris is not clogging the suction ports. The speculum, drapes, and lashes should be inspected to insure they are not impeding contact between the suction ring and the globe. Additional anesthetic can be applied to improve suction between the ring and globe. If these items appear normal, the suction line should be changed to insure it is free of defects. Chemotic or redundant conjunctiva may also obstruct the suction port on the ring, especially if the globe is small. In this situation, a smooth-surfaced instrument can be used to push away the subconjunctival fluid just prior to application of the ring. If everything else has been excluded, it is useful to have a back-up power/suction component so that proper function of this unit can be confirmed.

There have been no reports of retinal vascular complications caused by the relatively high intraocular pressure required in this procedure. This possibility is still a concern in patients with systemic diseases known to compromise the circulation.

MICROKERATOME-RELATED COMPLICATIONS DURING FLAP CREATION

Lamellar refractive surgery has several advantages over photorefractive keratectomy: less postoperative pain, quicker visual recovery, and no corneal haze overlying the entrance pupil in uncomplicated cases. However, flap complications are inherent to the surgery and have the potential to produce serious visual loss.

The frequency of flap complications is higher early in the “learning curve” and can be reduced with experience and attention to detail. However, flap complications still occur, even in the hands of the most experienced surgeons (Marinho A, Pinto MC, Pinto R, et al. LASIK for high myopia. Ophthalmic Surg Lasers 1996;27(suppl):S517-S520; Bas AM, Onnis R. Excimer laser in situ keratomileusis for myopia. J Refract Surg 1995; 11(suppl):S229-S233).19-25

Flap complications may range from insignificant to catastrophic (Fig 4A). The incidence of all LASIK complications reported in the literature ranges from 0.7% to 11.8% (Bas AM et al, 1995, cited above;
Kremer FB, Dufek M. Excimer laser in situ keratomileusis. J Refract Surg 1995;11(suppl):S244-S247; Fiander DC, Tayfour F. Excimer laser in situ keratomileusis in 124 myopic eyes. J Refract Surg 1995;11(suppl):234-238. Recent studies with large sample sizes of 1062, 1019, and 3998 eyes reported an intraoperative complication rate of 2.1%, 2.2%, and 0.68 %, respectively. Newer microkeratomes such as the Hansatome, with closed heads that pivot on a pin, have been shown to be safer than microkeratomes with paired tracks. Flap complications may be reduced to as low as 1 in 500 to 1 in 1000 cases with appropriate patient selection in the hands of an experienced and talented surgeon using a well-designed instrument.

It is important to prepare the patient for a potential flap complication prior to surgery. Our custom is to remind the patient that a flap complication can occur and that in the event of an irregular flap, no laser ablation will be performed. This preparation will prevent the patient from panicking in the event of a flap abnormality and reduce the chance that the surgeon will feel pressured to go ahead with the ablation when it is not appropriate to do so.

Irregular flap cuts rarely lead to significant visual loss and generally do not result in a change in refractive error unless the surgeon proceeds with the ablation. Most of the time the procedure can be repeated a few months later. The sections that follow detail some of the specific microkeratome-related complications that occur and discuss approaches to management.

**Eyelid Complications**

With some microkeratomes it is possible to nick the eyelid during flap formation. For example, this may occur with the Hansatome. Typically, this is a small superficial scrape or cut that heals without sequelae. The best way to avoid this trauma to the eyelid is to obtain excellent exposure with the eyelid speculum. With the Hansatome, the incidence can be reduced to nearly zero by rotating the handle of the suction ring gently toward the surgeon while placing the head on the pin and moving the microkeratome head into position. This maneuver lifts the gear track away from the lid. As the microkeratome begins its passage, the handle is returned to the upright position. After completing the flap,
the handle is again rotated toward the surgeon as the microkeratome head returns to the starting position. It is also useful to retract the lower eyelid inferiorly with the blunt end of a forceps.

**Incomplete Flaps**

Occasionally, the microkeratome head will stop prior to clearing the 6- to 6.5-mm diameter zone needed for unhindered ablation. Application of the laser treatment with such a flap will result in nasal flattening and irregular astigmatism, even if the hinge of the flap is protected from the laser beam (Fig 4B). Our practice is to return the flap to the bed without ablation unless there is at least 1 mm of bed between the intended ablation periphery and the flap edge in eyes with myopia. It is necessary to protect the hinge from the ablation in LASIK for hyperopia. This does not appear to have a significant effect on the quality of correction.

Some surgeons attempt manual extension of the flap using a lamellar dissecting blade. We believe this should not be done.

**Thin Flaps and Donut-shaped Flaps (Buttonholes)**

Flap buttonholes are more likely to cause loss of best spectacle-corrected visual acuity than free or incomplete flaps. Preoperative mean corneal curvature greater than 48.00 D and previous ocular surgery, such as corneal transplantation, are the most important risk factors. Any reduction in intraocular pressure during passage of the microkeratome increases the chance that there will be a thin or donut-shaped flap.

Surfacing of the blade during creation of the flap, resulting in a donut-shaped flap or a cut through the central cornea, is often associated with scarring or epithelial ingrowth into the interface that may compromise the surgeon's ability to successfully repeat the LASIK procedure at a later time (Fig 4C). If the lamellar cut was superficial, then the excimer laser can be used to eliminate the epithelial or scar opacity within the central cornea and rehabilitate the eye by performing a no-touch transepithelial PRK. This technique is most successful if used within the first few weeks following the complicated procedure before scarring or epithelial ingrowth become advanced. Delaying until a dense scar has formed will predispose to irregular astigmatism because the scar will ablate differently with the excimer laser compared with the adjacent clear stroma. The best approach is to protect the irregular flap with a bandage contact lens and proceed when the best spectacle-corrected visual acuity is nearly at the preoperative level or has stabilized for 2 to 3 weeks. With this approach, the thin corneal cap or flap and associated epithelial growth or scarring can be eliminated over a 6-mm-diameter area of central cornea. Residual lamellar tissue in the periphery remains in place and usually has no effect on vision. In the case of low myopia or hyperopia, it may be necessary for the surgeon to utilize a combination of PTK and hyperopic ablation to eliminate an offending flap defect. In some cases, more than one procedure separated by months may be required to eliminate the central cut or donut-shaped flap and provide sufficient refractive correction to prevent anisometropia. During the interval between procedures, we use a soft contact lens to improve the patient's function.

A central corneal scar associated with a transverse cut that emanated from what was a normal 140- to 180-µm-deep lamellar cut cannot, in most cases, be addressed with transepithelial PRK. This is because corneal tissue removal would be excessive and predispose to ectasia. A gas-permeable contact lens may be of benefit. In some cases, however, a rotational autograft or penetrating keratoplasty may be needed to restore vision.

**Decentered Flaps**

Decentered flaps can be as problematic as decentered ablations. Performing an ablation with a decentered flap, even if the ablation is centered on the entrance pupil, may yield unpredictable spherical and astigmatic corrections. Typically, flap decenterations are attributable to an inexperienced surgeon improperly aligning the suction ring with the limbus or migration of the ring on the corneal surface when suction is applied. When placing the suction ring, the surgeon should confirm the position of the inferior limbus and strive to maintain the base in that position while suction ramps up through posterior pressure on the suction ring. Suction should be turned off at the first sign of migration of the microkeratome ring so that a deep impression gutter is not formed. Such a gutter will tend to repeatedly return the suction ring to the decentered position. Sometimes the surgeon must wait for 5 to 10 minutes for such a gutter to disappear prior to proceeding. Occasionally, it is necessary to intentionally decenter the microkeratome suction ring in the opposite direction a small amount so that when suction is applied, migration stops in the appropriate location. Rarely is it necessary to cancel the case and come back on another day.

Corneal contour appears to have some role in decentation of the flap. If the microkeratome ring
has a tendency to decenter in one eye, a tendency to decenter in the same manner (nasal or temporal) is commonly present in the second eye. Slight decentration in the direction opposite to the anticipated migration is often helpful in obtaining centration after the suction is applied.

In the event that a decentered flap is formed, we follow the guideline of not proceeding unless the ablation can be placed so that 1 mm of bed is left between the ablaton peripheral edge and the flap margin. There may be major changes in the contour of the cut in the 1 mm of stromal bed next to the flap margin, and incorporating this area into the ablation may induce unpredictable refractive results. It is not clear why this should occur if the flap is of plano power, but we have noted this in several cases. Perhaps the augmented wound healing response at the edge of the flap is a factor.

One of the developments that has reduced this problem has been the introduction of microkeratomes with larger diameter flaps. This is one of the reasons we prefer newer microkeratomes such as the Hansatome, the Moria Carriazo-Barraquer (Paris, France) or the Innovatome. If significant decentration of the flap is noted, the best course of action is to return the flap to its original position and repeat the procedure 3 to 6 months later.

**Free Caps**

Occasionally, a surgeon will find that an inadvertent free cap has been produced. This is most likely to occur with corneas flatter than 38.00 D prior to surgery. In some cases, the cap is not visible on the surface of the cornea. If this occurs, the microkeratome head should be disassembled carefully since the cap is probably inside the instrument. If the cap has normal thickness and diameter, the excimer laser ablation can still be performed with excellent results. Replacement of the cap in its original position with the epithelium up is facilitated if the surface was marked for orientation prior to surgery. Severe irregular and regular astigmatism are common if the surface was not marked and the cap ends up rotated relative to its original position. The few moments that are required for marking the flap is insignificant compared to the amount of time and anxiety the surgeon will expend on one of these complicated cases. In rare cases, sutures are needed to anchor a free cap that will not adhere or becomes displaced. Sutures should be removed as soon as the epithelium heals to minimize scarring.

In the event one is faced with an apparently erroneously positioned cap, it may be possible to approximate the appropriate position (Robert Maloney, MD, unpublished data, 2000) by remembering the optical rule that when a corrective cylinder is placed off axis, a new cylinder is introduced at an angle of 45° to the bisector between the true cylinder axis and the axis at which the corrective cylinder is erroneously placed. In some cases, more than one attempt at repositioning may be required to align the flap near its correct position.

**Erroneous Microkeratome Assembly**

A potentially catastrophic complication of LASIK is human error in failing to place the plate that controls depth of cut into instruments, such as the Automatic Corneal Shaper. This omission has unfortunately occurred in several cases reported at meetings. It results in perforation of the cornea and entrance into the anterior chamber in an eye pressurized to more than 65 mmHg, causing serious damage to the iris, lens, ciliary body, and other structures in the eye. It is critical that the surgeon never engage the microkeratome head without checking for the presence of a correctly positioned depth plate.

Other microkeratomes that are currently on the market can also be assembled incorrectly and still function to produce a flap. For example, when this occurs with the Innovatome microkeratome, a thick flap is produced. This is unlikely to be detected by the surgeon until drops of aqueous humor appear during the ablation. Although the cornea may recover from the localized endothelial damage in the center of the ablation, these corneas are likely to be at risk for developing ectasia, since the remaining posterior bed is limited.

Corneoscleral perforations have also been reported to occur during formation of a corneal flap. This may result in vitreorelinal complication.

Newer designs, such as the Hansatome and the Carriazo-Barraquer (from Moria) have eliminated the potential for these severe complications since they have a fixed depth plate and components of the microkeratome cannot be inserted incorrectly to produce a functional microkeratome. Before purchasing any microkeratome, we recommend determining whether the instrument will function if any of the components are inserted incorrectly. If use following improper assembly is possible, then the instrument should be avoided.

**Intraoperative Bleeding**

Intraoperative bleeding at the edge of the flap tends to be more of a nuisance than a complication.
Bleeding of the perilimbal corneal vessels has been reported as the most frequent complication of LASIK performed by an experienced surgeon (Velasco-Martínez EJ, Tarcha FA. Superior hinge laser in situ keratomileusis. J Refract Surg 1999;15(suppl):S209-S211).

This occurs most commonly with wide diameter flaps. MacRae and colleagues presented two cases in which blood entered the interface after a small hemorrhage from peripheral corneal vascularization after formation of the flap. Although bleeding was controlled and all visible blood cells were removed at the time of surgery, both patients developed a focal interface keratitis on the first postoperative day.

The most common cause of intraoperative hemorrhage is corneal neovascularization from pannus related to long-term contact lens wear. The micropannus is usually superior. Other causes are decentration of the microkeratome and a small corneal diameter relative to the diameter of the microkeratome. Preoperative examination should include detection of pannus and the extent to which the vessels encroach into the peripheral cornea so that precautions may be taken. The preoperative use of topical vasoconstrictors like neosynephrine and naphcon can be considered. We typically apply vasoconstrictor only in those cases where we suspect there will be bleeding, and wait 3 to 5 minutes prior to proceeding. Once the flap is formed, it is also helpful to wait approximately 1 minute before lifting the flap if bleeding is detected. This will tend to tamponade the vessels. In the event that the blood approaches the ablation zone, it may be necessary to interrupt the ablation to clear the blood with a sponge before proceeding.

Bleeding can rarely be extensive and difficult to control. In such a case, returning the flap to its original position while irrigating the interface with balanced saline solution (BSS) will typically clear the blood from the interface and tamponade the vessels. In our experience, the ablation can almost always be completed prior to this maneuver. Significant bleeding is so rare that we typically avoid decentering the flap to avoid localized micropannus because of the risks outlined in the previous section. A BSS moistened Chayet sponge drain (Ultracell, North Stonington, CT) is also an option for managing these rare cases during ablation. The sponge is placed around the flap so that any bleeding is wicked away from the flap edge.

Intersecting Microkeratome Cuts and Other Irregular Flap Cuts

When a LASIK flap is recut, there is a risk of intersection between the new interface and the original interface. When this type of intersection occurs, a sliver or disc of stromal tissue may be produced. Displacement of these amputated tissue pieces may result in irregular astigmatism that cannot be corrected unless the proper position can be found. Recutting with a Hansatome following an original Automated Corneal Shaper flap has been reported to be associated with a high risk of these complications. It may be helpful to use a deeper cutting microkeratome for the second flap, however, this does not eliminate the possibility of an intersection because of the variability in true flap thickness relative to the specified thickness with all microkeratomes.

Most flaps can be lifted 5 to 7 years after surgery. The authors believe this should always be attempted prior to considering recutting of the flap. At times the healing is so extensive that lifting is not possible and recutting must be considered. It may be better to avoid enhancement in these cases.

Atypical flap cuts may also be noted after corneal transplantation, radial keratotomy (RK), arcuate keratotomy (AK), or automated lamellar keratoplasty (ALK). In the authors’ experience, flap complications attributable to prior corneal transplantation, RK, or AK, occur at increased frequency relative to corneas that have not had previous surgery, but still are relatively rare if incisions are well healed. We wait at least 1 year after the incisional procedure before considering LASIK.

If slivers, free discs, or other anomalies of the stroma are noted after microkeratome passage, the surgeon should make every effort to return the stromal components to their original position in an attempt to limit irregular astigmatism that commonly occurs in these situations. Never discard free tissue pieces. Future reposition procedures designed to reduce induced irregularity can only be undertaken if the fragments are retained. Take the time to try to reapproximate the pieces and protect the surface with a bandage contact lens for the first day to increase the chance of an acceptable outcome.

Other Microkeratome-related Problems

Blade chatter is occasionally noted when the flap is lifted and the bed is examined. In some cases this
may be attributable to a blade defect or jerky transition of the micokeratome head. In our experience, such chatter is rarely of visual significance since it is typically mild and even after ablation the posterior surface of the flap and the bed tend to reapproximate. However, if the chatter is extensive, the flap should be replaced without performing the ablation. The procedure can be repeated after approximately 3 months. These types of flap irregularities can be reduced by careful inspection of blades for defects (Fig 5) and avoiding reuse of blades for different patients.

EXCIMER LASER ABLATION-RELATED COMPLICATIONS

Temperature, Humidity, and Input Errors
The laser suite environment is critical for optimal performance of the excimer laser. The manufacturer’s recommendations for temperature and humidity should be strictly followed if a precise nomogram is to be produced and maintained. It may be necessary to install a humidity and temperature control system in the operating suite to achieve this uniformity.

The excimer laser must be monitored for appropriate alignment and ablation profile at regular intervals. All laser manufacturers provide guidelines specific to their instrument. Test plates are available to independently evaluate ablation profiles. Lack of homogeneity can be attributable to expected wear on the excimer laser optics and may result in undercorrection, overcorrection, or other anomalies such as central islands.

A nomogram should be established for individual lasers and surgeons for optimal accuracy and precision in laser correction. Even surgeons using the same laser in a single operating suite will frequently have differing outcomes based on variations in technique. Once established, a nomogram should be continually monitored for variations that may occur with differing humidity, optics changes, and other factors.

Erroneous computer input is a common source of error in the application of laser energy in performing LASIK or PRK. Undercorrection attributable to operator error can be corrected by enhancement. Overcorrection to hyperopia and axis misalignment may be difficult to correct. The surgeon should always verify input into the excimer laser before beginning ablation. At our center, the surgical plan is positioned in front of the surgeon adjacent to the laser terminal. Correct input of the parameters is verified by direct surgeon observation. This simple approach will eliminate many input errors.

Hydration of Tissue
Hydration of the stromal bed should be rigidly controlled. For example, if the surgeon typically sponges the intended ablation zone with a dry or moist sponge, this practice should be rigidly followed in generating and following the excimer laser nomogram.

It has been mentioned that excessive topical anesthetic will also alter hydration of the corneal stroma due to effects on epithelial barrier function. In addition, fluctuation in the time between first application of the anesthetic and laser ablation is a source of inconsistency in stromal hydration. Our practice is to apply a single drop of anesthetic just prior to prepping of the eye. Once the prep for the individual eye is completed, another drop of anesthetic is applied and LASIK is performed immediately.

Decentration of Ablation
Decentration of ablation is a common complication in LASIK patients (Fig 6A). This is most common in cases performed by inexperienced surgeons where insufficient attention is paid to centering the laser mires on the entrance pupil. All refractive surgical procedures should be centered on the entrance pupil. The ablation should be stopped immediately and the mires repositioned prior to proceeding if deviation from the pupil is detected. An eye tracker that follows eye movements may be useful, but even this is not foolproof. Patient cooperation and fixation are still critical to alignment of the entrance pupil to the line of sight.37 There have been a number of reports of decentered ablation using lasers with trackers that are typically attributable to
Centration is especially critical in the treatment of hyperopia. The steepening induced by treatment of hyperopia may result in induced astigmatism and poor visual quality unless centration is optimal. The higher the level of correction, the more critical centration becomes. For this reason, and because regression may also induce irregularity, we limit hyperopic LASIK correction to less than +4.00 D.

Some measures can be taken to improve patient fixation. First, careful instruction should be given to the patient to ensure that he or she has correctly identified the fixation target. Microscope and room lighting should be reduced to a minimum. We have observed that elimination of sedation with Valium and other medications significantly improves patient attention. In our experience, such sedatives are rarely needed.

**Topographic Central Islands and Peninsulas**

Excimer lasers damage their own optics by slowly ablating the glass. Such degradation results in inhomogeneity of the ablation. One of the most common complications is a central island (Fig 6B) attributable to a cold spot in the center of the optics, although virtually any anomaly is possible. Peninsulas (Fig 6C), off-center islands, divots, and other abnormalities can occur. Optics should be monitored according to the manufacturer’s protocol. Our preference is to perform calibration after every two or three eyes. The surgeon should be prepared to terminate treatment at the first sign of problems.

It is important that patients be informed of the possibility of cancellation in the event of equipment malfunction prior to the day of surgery so that they are prepared for unexpected rescheduling.

A common cause of ablation irregularity is a drop of moisture falling on the ablation zone during lifting of the flap. It is important to dry the flap margin with a sponge just prior to lifting. Any drop that falls on the ablation zone immediately changes the hydration at that point, resulting in irregular hydration across the ablation. Even immediate...
drying with a sponge will not completely eliminate this spotty hydration, although this still should be done. This irregular hydration may result in irregularity of the ablation. The splashing of fluid from the cornea onto the laser lenses can also damage the optics.

Ablation zone irregularity will typically produce symptoms of poor vision quality, monocular diplopia, halos, and starbursts. These can be difficult to treat. In some cases, the abnormalities will decrease or disappear over time. If they persist and the irregularity is not likely to be attributable to flap striae or other surface problems, then an attempt at smoothing can be made. Our preferred technique is to lift the flap, as in preparation for an enhancement. Then, a small drop of Healon (Pharmacia, Peapack, NJ) diluted to 0.2% sodium hyaluronate (1:5) with BSS, is applied to the ablated zone and immediately smoothed over the zone with a spatula so that there is a thin film. The solution will tend to fill the valleys and expose the peaks of the irregularity. The broadbeam laser in phototherapeutic (PTK) mode with a 6.0-mm ablation zone is then centered on the entrance pupil and a few bursts are applied. The smoothing agent is distributed again with the spatula and a few more bursts of PTK are applied. This maneuver is repeated 5 to 10 times. A decrease in the irregularity of the surface is obvious at the time of surgery when this technique is performed properly. The bed is then irrigated with BSS and the flap returned into position using the same technique as with enhancement. This treatment can be repeated and in some cases eliminates or markedly improves the patient's symptoms.

Epithelial Complications

Flap epithelial defects occur only in a small percentage of eyes when appropriate technique is used in performing LASIK. Epithelial defects can cause pain and photophobia. They also prolong visual recovery. The risk of infection is also increased. Some surgeons believe the incidence of epithelial ingrowth is significantly higher in eyes with an epithelial defect on the flap. Flap displacement may also be more common because of alterations in flap adhesion. Diffuse interface keratitis may be triggered by an epithelial defect. Wetting the surface of the cornea with proparacaine just prior to passage of the microkeratome seems to decrease the incidence of epithelial abrasion. Use of a salt containing solution prior to the ablation should be avoided because of potential damage to the microkeratome motor and gears. Patients with epithelial adhesion abnormalities are especially prone to epithelial defects.

In the authors' experience, an epithelial defect does not necessarily predispose to a poor outcome. Regression—likely related to an augmented wound healing response—is frequently noted in these eyes. Use of a bandage contact lens increases patient comfort and may decrease the frequency of related flap displacements or epithelial ingrowth. If an epithelial abrasion occurs in the first eye of a patient, then there is a high likelihood of occurrence in the second eye. Thus, if there is a large abrasion, it is prudent to postpone treatment of the second eye.

POSTOPERATIVE COMPLICATIONS

Pain
Most patients experience only mild discomfort following LASIK. Typically, this manifests as mild burning or stinging lasting for a few hours after surgery. A foreign body, gritty, or dry sensation is commonplace. As with any surgical procedure, variability in tolerance plays a significant role in determining the level of these subjective symptoms. Complaints of severe pain may herald more severe complications such as a displaced corneal flap, diffuse lamellar keratitis, or infection. Thus, severe pain on the night of surgery or even mild pain more than 1 day after surgery warrants an examination. Nonsteroidal anti-inflammatory agents and bandage contact lenses reduce perioperative discomfort. Rarely do patients need narcotic analgesics for a few days after surgery. Lubrication is another important adjuvant since many of these eyes have mild neurotrophic epitheliopathy or underlying dry eye.

Patients frequently report dysesthesias for months or even years after LASIK. Such patients report discomfort on pushing on the globe through the eyelid. This is likely attributable to deinnervation hypersensitivity associated with the cutting and incomplete regeneration of the corneal sensory nerves. This sensation seems to diminish over time, but in some cases may never completely resolve. No other sequelae have been associated with this sensation.

Postoperative Flap Striae and Wrinkles
Flap striae or wrinkling is relatively common after LASIK (Fig 7). Fortunately, most striae do not appear to significantly affect the quality of vision. Striae are most commonly related to disparity between the curvature of the posterior surface of the flap and the bed following ablation. Thus, the
incidence of striae appears to increase as the level of correction increases. Alternatively, striae may be introduced during the procedure by touching the flap with a sponge, improper insertion of a contact lens, removal of an eyelid speculum, or some other manipulation. Many of these striae are not detectable with the operating microscope, prompting some surgeons to inspect the flap at the slit lamp immediately after surgery. In other cases, striae may not be detected until 1 or more days following surgery. These late occurring striae are presumably due to patient eye rubbing, pressure on the eye while sleeping without a protective shield, the patient touching a drop applicator to the cornea, eyelid blinking that partially dislodges the flap, or some other mechanism.

Every effort should be made to eliminate flap striae as soon as they are identified and deemed to be visually significant so that permanent irregular astigmatism can be prevented. Frequently the patient will report visual abnormalities that correlate with striae as early as the day after LASIK surgery. This should prompt immediate intervention, since the longer striae are present, the more difficult they are to eliminate. Any reduction in best spectacle-corrected visual acuity present 1 week after surgery should dictate careful inspection for striae that may be difficult to detect at the slit lamp. In many cases, these are detectable by inspection of the red reflex with a funduscope. Immediate intervention is advised if visually significant striae are detected.

Technique for elimination or reduction of striae should include lifting of the flap. We believe that it is less traumatic to rest the flap against the superi- or conjunctiva rather than a sponge or metal spatula. The flap should be irrigated profusely (3 to 5 cc) with sterile solution and smoothed with repeated stroking of the posterior surface with a rounded spatula. Gentle stretching of the flap with a pair of forceps may be helpful. It is our preference to utilize a relatively hypotonic saline solution such as 50% balanced salt solution diluted with sterile water to promote hydration of the flap due to the difference in osmotic pressure between the tissue and the solution. Some have advocated merely using sterile water for this irrigation, but such a wide disparity in osmotic pressure, and the dramatic reduction in tissue osmotic pressure, are likely to be more toxic to both the epithelial cells and keratocytes. Other surgeons believe that use of phosphate buffered saline is sufficient.

Once the flap is returned to the stromal bed, further smoothing can be performed by stroking the surface of the flap with a moist sponge while taking advantage of the tethering effect of the hinge. Finally, a bandage contact lens should be placed into position to help prevent displacement of the hydrated flap.

In our experience, only marginal improvement in the appearance of the striae is noted immediately following these maneuvers, but striae are often completely eliminated the next day. This is especially likely if intervention is performed within approximately 1 week of the original procedure. Presumably this indicates that further swelling of the flap occurs in the hours following the procedure. Some surgeons have advocated gently scraping away the epithelium overlying the striae at the time of this intervention to “release traction.” This could
be useful in some cases, especially when intervention has been delayed, but there is increased risk of diffuse lamellar keratitis (DLK) associated with the epithelial defect. We have not been impressed with “flap irons” and other devices used to press out striae without lifting the flap. Some surgeons, however, have reported these instruments to be useful.

We believe it can be helpful to attempt removal of striae regardless of how long they have been in place. In some cases, subjective symptoms are improved despite little apparent improvement in the appearance of striae.

At times it is impossible to eliminate flap striae or even reduce them substantially. It may be necessary to fit a gas-permeable contact lens to improve visual function if symptoms persist despite attempted removal.

**Postoperative Flap Displacement**

Flap complications such as displacements may also occur following surgery. In fact, Stulting and colleagues\(^22\) noted that postoperative flap complications were almost two times as common as intraoperative flap complications. Thus, a flap my be displaced or lost in the first few days after LASIK. However, flap displacement occurs most commonly in the first 24 hours following LASIK, before the epithelium has had time to heal over the lamellar entry site. This is why the first postoperative day examination is so critical that it should be performed by the surgeon. This, however, is controversial.

There are many potential causes of flap displacement. Not allowing sufficient time for the flap to adhere to the bed is one potential cause. The optimal time is not known, but is likely to be related to the overall technique. For example, despite irrigation of the flap and bed, we have found that 1 minute is sufficient if the flap is protected with a contact lens. Recommendations of other surgeons vary from 30 seconds to 5 minutes. The central cornea should be maintained moist and the periphery dry to facilitate adhesion of the flap to the bed.\(^20\)

There is controversy regarding the mechanism of flap adhesion. Some speculate it is attributable to endothelial pumping with return of the flap to its original position and restoration of epithelial barrier function. We believe that a much longer period of time is needed to restore hydration equilibrium in the stroma following irrigation of the flap and bed. We believe that the flap is most likely held in position the first day following surgery by simple tissue adhesion.

Although rare, the corneal flap can be displaced from the bed many years following LASIK. Lemley, and colleagues\(^41\) reported a patient who developed partial dislocation of the flap from air bag deployment 17 months after LASIK. Patients should also be told to avoid holding an infant, participating in sports, or other activities that could lead to flap displacement by a finger or other object for several days after surgery. It is a good policy to advise patients to wear safety glasses in any environment in which they could be struck in the eye for several weeks after LASIK.

Flap displacement can be caused by excessive pressure patching of the eye, patient rubbing of the eye, or the posterior margin of the eyelid catching the edge of the flap and flipping the flap out of position. Use of a soft contact lens, without patching, on all eyes for the first 24 hours after LASIK or enhancement may reduce the incidence of flap displacement. Using this technique, we have had only two displacements out of a total of more than 3000 cases, both during the first 24 hours following surgery. We recommend the Bausch and Lomb Soflens 66 F/M base curve contact lens. Even after LASIK for -12.00 D or more, or +6.00 D, this contact lens usually fits well. The rather wide diameter of the contact lens allows it to act as a glide to prevent the eyelid from catching on the edge of the flap until the epithelium has closed. Use of superior flap hinges that can be created with the Hansatome, Moria, and other microkeratomes may further decrease the incidence of this complication since the upper lid is less likely to catch on the edge of the flap.

Loss of the flap is relatively rare. It may still occur, however, in the case of an inadvertent cap or even with a flap if displacement occurs and the hinge is severed by blinking. If the cap cannot be located, severe irregular astigmatism and unpredictable refractive change may occur. Some surgeons have reported treating this complication by crafting a new cap from a donor eye. The pressure in the donor eye must be increased by fluid injection. The microkeratome can then be used to form a new cap.

**Epithelial Growth Within the Lamellar Interface**

Ectopic epithelium growing within the LASIK lamellar interface can produce significant morbidity.\(^20,22,41-43\) The term epithelial ingrowth may not be appropriate in many cases since epithelial debris may be implanted by the microkeratome blade during flap creation.

The frequency of this complication appears to vary from surgeon to surgeon and the associated...
LASIK Complications/Ambrósio and Wilson

Factors are poorly understood. In a recent study of 1013 eyes by Stulting and coworkers\(^{22}\), 14.7% were reported to have epithelial growth within the interface, with 1.7% of all of the eyes in the study requiring surgical intervention for epithelial ingrowth. Conversely, in a recent study of 783 consecutive eyes that had primary LASIK and 108 eyes that had LASIK reoperation, only three eyes developed epithelial growth within the interface.\(^4^3\) Only one of these cases required intervention by the surgeon. The reason for this major difference in incidence between the two series is not clear. Stulting and coworkers\(^{22}\) asserted that patients with anterior basement membrane dystrophy were at increased risk, but the other study did not note this association.

Precautions taken at the time of surgery can lower the rate of epithelial growth within the interface. A discussion of factors that may be associated with this complication and precautions that can be taken to prevent it will provide some insight.

Epithelium within the interface is a potential complication of all lamellar refractive surgical procedures, including LASIK, automated lamellar keratoplasty (ALK), and epikeratoplasty. When the microkeratome blade cuts through the peripheral epithelium, there will always be some epithelial tissue that adheres to the blade. This epithelial tissue may be deposited within the interface during passage of the blade. Reusing a blade for multiple flaps may increase the likelihood that this will occur since the blade will become dull. If the epithelial tissue contains viable cells, then these cells may proliferate and produce a nest of tissue within the interface. Most of the time these cells will have limited proliferative potential and, if so, a nest of cells may appear, stop expanding, and remain stable for years within the interface. Occasionally, the nest of cells will continue to expand and may produce more significant complications that dictate intervention.

The most common mechanism of epithelial growth within the interface is ingrowth from the periphery. This may be related to the morphology of the flap edge with the incidence being lower in eyes that have a flap with a scalloped edge, such as that produced with the Hansatome microkeratome. In other cases, a minor flap edge lift, for example by the eyelid, may allow a peripheral tongue of epithelium access to the interface. Alternatively, the surgeon may not detect a tongue of epithelium that is lying on the peripheral bed and replace the flap so that this tissue is captured beneath the flap. This is a common mechanism with LASIK enhancements.

Finally, epithelium may grow into the interface from a central defect in the flap or cap. For example, when a thin donut-shaped flap is produced or the flap has a split in the center, there is increased risk that epithelium can grow down from the surface and into the interface.

Epithelial growth within the interface can be held to a minimum by taking a few precautions at the time of surgery. There are many excellent techniques for LASIK. One technique will be described here to illustrate steps that may be helpful in preventing epithelial growth within the interface. An aspirating lid speculum, which attaches to suction with ports adjacent to the conjunctival surface, is helpful to remove tears, epithelial debris, and mucus from the fornix. An aspirating lid speculum also allows liberal irrigation to eliminate any implanted epithelium. Aspirating specula are commercially available from several sources. After the laser correction is applied to the stromal bed, the flap and bed are irrigated with BSS delivered with a smooth-tipped cannula with an attached 0.2-μm filter. The cannula tip is used to dislodge any debris that is not visible on both the flap and in the bed during irrigation. This may be followed by a brief sweeping of the bed and flap with lint-free sponges (for example, a Merocel sponge, Solan Ophthalmic Products, Jacksonville, FL). This sponge maneuver is designed to remove epithelial debris that is not visible through the operating microscope. Finally, the bed and flap are irrigated one final time with filtered BSS, prior to smoothing the flap back into position.

Other surgeons have different approaches. Another common technique is to wait to irrigate the lamellar interface after the flap has been rotated back into position. A cannula is inserted beneath the flap and profuse interface irrigation is performed with filtered BSS. A recent study with a relatively low rate of epithelial growth within the interface after LASIK used this method.\(^4^3\)

Some method of irrigation after flap preparation is useful not only for reducing the incidence of epithelial debris and other foreign materials within the interface, but also to dilute agents that might cause diffuse lamellar keratitis.

LASIK enhancement may be associated with a higher risk of epithelial growth in the interface, especially if a spatula is inserted through the epithelium and used to break open the interface by sweeping along the flap edge. Epithelial tissue will adhere to the spatula and be transferred onto the interface using this approach. If some of these cells
are viable, they may grow. Even though they are not stem cells, they may be transient amplifying cells with considerable proliferative potential. It is preferable to break open the interface at a single clock hour 180° from the hinge, grasp the edge of the flap gently with 0.12 forceps or smooth curved forceps, and gently peel back the flap. This will typically give a smooth edge of epithelium and limit introduction of epithelium into the interface. Any prominent adhesions between the flap and the bed can be broken with a dry, lint-free sponge. Otherwise, interface precautions are identical to those for the primary LASIK procedure.

If epithelial growth within the interface is noted following LASIK, then treatment is dependent on the extent and location of the ectopic epithelial tissue. A small nest of epithelium that is present in the periphery can be left alone (Fig 8A) if it does not progress or affect visual acuity (ie, by lifting the flap to induce irregular astigmatism). Clinically significant epithelial growth within the interface can affect vision by two primary mechanisms. First, it may grow to infringe on or cover the pupil (Fig 8B). If the epithelium within the interface continues to grow and threatens the pupil, then the flap should be lifted and the epithelium removed. A more common complication of epithelial growth within the interface is induction of irregular astigmatism because of localized lifting of the flap. This can produce a pseudodecentration on corneal topography. A decrease in best spectacle-corrected visual acuity or uncorrected visual acuity attributable to effects of the interface epithelium on the flap should prompt intervention. Some patients also experience a foreign body sensation when there is epithelial ingrowth at the flap margin. This is an indication for removal of the epithelium, even if it is confined to the periphery.

Rarely, epithelium within the interface can induce tissue necrosis in the overlying flap or melting of the edge of the flap. This is caused by the anterior stroma of the flap being deprived of nutritional factors derived from the aqueous humor. The first sign of impending necrosis is often inflammation in the stroma overlying the area of ectopic epithelium. A spontaneous epithelial defect occurring on the surface above a nest of epithelium is another danger sign. Detection of inflammation or a spontaneous epithelial defect should prompt immediate removal of the epithelium from the interface.

Typically, the epithelium can be scraped gently from the bed and flap with a scalpel or spatula. Some have advocated only lifting the sector where the epithelial ingrowth is located. We believe lifting the entire flap provides better access and decreases the chance that irregular astigmatism will be induced by asymmetric lifting of the flap. Once the nest of epithelium is removed, the interface should be irrigated with filtered BSS and cleaned with a lint-free sponge, as was described for primary LASIK.

Epithelial ingrowth may recur—although rarely—after repeated removal. In these rare cases, manual removal of the epithelium can be augmented with a dusting of both the bed and posterior flap surfaces with the excimer laser in PTK mode to ablate nests of cells that cannot be seen. Care must be taken when using the laser with this technique so that severe irregular astigmatism is
not induced by overlapping, multiple laser bursts. Central corneal ablation should be performed, centered on the entrance pupil. Only three or four pulses of the laser are required to irradiate a monolayer of epithelial cells. Since the visible epithelium will have already been removed with a spatula or scalpel, only a few pulses should be used. It is rare that there is a need for this laser augmentation.

Lamellar Interface Debris

Foreign materials may be introduced beneath the flap during the LASIK procedure. These include mucous or oil from the tear film, metal shavings or other materials from the microkeratome blade, particles from a sponge, red blood cells, and lashes. No lubricating oils or other liquids should be used on the microkeratome because they can contaminate the interface.

Small particles that are in the periphery and not associated with keratitis or corneal vascularization can be left undisturbed. If foreign bodies overly the entrance pupil should probably be removed.

Regular Astigmatism

Changes in regular astigmatism are common after LASIK. In some cases, uncorrected visual acuity will be limited by regular astigmatism, even though the spherical equivalent refraction of the eye has been corrected to plano. In these cases, toric enhancement can be performed to decrease regular astigmatism. If the surgeon works in a location where hyperopic astigmatism ablation is not available, then astigmatic keratotomy (AK) remains an option.

Some surgeons have used AK beneath the flap at the time of the primary LASIK procedure. However, there have been reports of serious perforations and resulting difficulty obtaining flap adherence with this technique. Our preference is to use AK as a later procedure when the spherical refractive error has been reduced or eliminated with LASIK.

Typically, AK is performed using a rectangular blade and the Lindstrom-Casebeer nomogram with an optical zone diameter of 7 mm. Since the initial blade setting with this nomogram is the central corneal thickness (that has been reduced by LASIK ablation) + 40 μm, the initial AK tends to be conservative. If necessary, re-cutting within the original incision is easily performed a few weeks later. Limbal AK is also an option for low levels of astigmatism.

Irregular Astigmatism, Glare, Halos, and Other Disturbances of Visual Quality

Irregular astigmatism and an associated loss of best spectacle-corrected visual acuity is a common complication of LASIK. There are many factors that contribute to irregular astigmatism following LASIK, including irregular flap cuts, flap misalignment, flap striae, ablation decentration, and epithelial growth within the interface.

A common irregularity that may be noted following LASIK is a central island or peninsula. There appears to be a tendency for central islands or peninsulas with LASIK than with PRK. To some extent, this may be related to the higher corrections that are attempted with LASIK. Another possibility is a “wetter” stroma at the level of LASIK relative to PRK. There also seems to be more of a tendency for fluid to accumulate in the center of the ablation during LASIK, resulting in excimer laser energy absorption by water rather than stroma. Anti-island software should be utilized with all broadbeam lasers. Scanning excimer lasers do not appear to have a proclivity to form central islands, although they have been noted in rare instances.

In the authors’ experience, there is little tendency for a central island to spontaneously resolve over time following the LASIK procedure. Thus, central islands associated with LASIK may be treated within a few months of the primary procedure.

To a large extent, treatment of islands and peninsulas remains an art. Attempts can be made to measure the diameter and height of the island and to enter a corresponding custom ablation into the excimer laser. However, caution should be taken in applying such a technique since computerized corneal topography instruments are notoriously inaccurate in making measurements in the center of the cornea. Thus, when using the topographic map to guide central island treatment, one should be conservative in applying treatment. In some cases, the flap must be lifted more than once to apply laser energy to eliminate a central island. Peninsulas are typically even more difficult to treat and usually attempts to eliminate them are unsuccessful.

Decentration can result in severe irregular astigmatism overlying the entrance pupil. This can cause glare, monocular diplopia or multiplopia, and halo phenomenon. Patient fixation tends to be more difficult after the flap is lifted. To some extent, this can be remedied by performing the ablation under the lowest possible illumination so that the
patient can see the fixation target. Thus, the illumination should be very dim, while still allowing the surgeon to monitor the entrance pupil upon which the ablation should be centered. For example, with the VISX S2 laser, the ring light should be turned off and the side illumination placed at its lowest setting just prior to beginning the ablation.

Once decentration has occurred, correction can be difficult and at present is more art than science. One difficulty is that there is no epithelium to use as a masking agent, as there is to treat decentration following PRK. Viscous agents such as methylcellulose or diluted Healon can be used to mask the area that has already been ablated, while attempting to reablate overlying the entrance pupil. Some surgeons have proposed using an identical ablation that is similarly decentered 180° in the opposite direction. Only anecdotal reports have demonstrated the efficacy of these approaches in eyes that have had LASIK. Hopefully, scanning lasers will eventually be able to perform custom ablations driven by real-time corneal topography and wavefront analysis. Until then, the best treatment is prophylactic reablation overlying the entrance pupil. Some surgeons believe that large pupil size is a risk factor for glare and halos.45 As the pupil dilates, it seems more likely that glare, halos, and other visual imperfections would be attributable to the junction between ablated and un-ablated cornea. However, we have noted many patients who have no glare or halos despite having a high correction with large pupils. On the other hand, we have had patients complain of glare and halos despite small pupils with a low correction. Clearly, other factors such as patient perception, centration, irregularity of the ablation, and irregular healing are also important. In general, however, we have a full discussion with the patient about the potential complications and are reluctant to offer LASIK to patients with high myopia (greater than -5.00 or -6.00 D) and pupils larger than 7 mm.

Pupillometers can be useful, but the room lighting must be standardized for the measurements to be meaningful. We have found that videokeratoscope images provided along with topographic maps on instruments such as the Humphrey 992 topographer are useful for estimating the size of the pupils and providing a permanent record. These videokeratoscope images are obtained with constant lighting and can easily be correlated with pupil size measured with a pupillometer.

Larger ablation diameters may be helpful in reducing these complications, although consideration...
demonstrated conclusively that wound healing associated with LASIK. Recent studies, however, have questioned the belief that there was no wound healing asso- ciated following LASIK. This followed from the erro-

Undercorrection and Regression

Early dogma claimed that there was no regression following LASIK. This followed from the erroneous belief that there was no wound healing associated with LASIK. Recent studies, however, have demonstrated conclusively that wound healing occurs following LASIK (Wilson SE. Role of apoptosis in wound healing in the cornea. Cornea 2000;19(suppl 1):S7-S12). It seems likely that regression in LASIK is attributable to stromal remodeling and/or epithelial hyperplasia. Sources of regression are thought to be a greater than average wound healing response or complications that promote healing. For example, a thin flap may be associated with regression since the stromal wound healing response and epithelium-modulating growth factor production are more likely to be in proximity to the epithelium. This probably promotes epithelial hyperplasia. Other factors such as epithelial defects produced by the microkeratome and diffuse interface keratitis are also likely to be associated with a stronger wound healing response and regression. The higher the level of correction, the more likely regression due to wound healing will occur. In our experience, regression is most common in hyperopic corrections, especially those over +5.00 D.

Fortunately, most regression that occurs following LASIK is treated easily by lifting the flap and reablating with the excimer laser. In the authors’ experience, most flaps can be lifted for years after the primary procedure. Some surgeons prefer to recut a new flap. This is easily done, but there is a higher risk of serious flap complications.

A surface ablation excimer laser technique can also be applied with caution in eyes in which there is concern about lifting an existing flap or cutting a new one. Transepithelial PRK can be applied to correct a small amount of myopia in these cases. It is probably wise to limit these PRK corrections to eyes with only a small amount of myopia (less than -1.50 D) that are at least 1 year removed from the primary procedure, since higher corrections have been associated with significant haze and regression. Care should be taken in applying this PRK enhancement method until more cases have been studied. Many surgeons believe it is contraindi-

Early regression of refractive effect after LASIK for myopia appears to be a consequence of an increase in corneal thickness that is probably due to thickening of the epithelium. Lohmann and colleagues reported regression related to postopera-

The study of the corneal microstructure using new methods like ultrasound biomicroscopy, optical coherence tomography, and confocal microscopy...
may give us important information such as the thickness of the cornea posterior to the flap. Such measurements can help the surgeon distinguish between epithelial hyperplasia and stromal remodeling as the cause of the refractive regression. 53

**Progressive Corneal Steepeening After LASIK**

Corneal steepening can occur after LASIK and may progress to ectasia, producing a keratoconus-like clinical appearance. Some reports suggest this is even possible after treatment of relatively low myopia. 54 It is especially important to detect early keratoconus or forme fruste keratoconus preoperatively since kerectasia may occur with rapid progression. 55,56 Geggel and colleagues 57 presented a case of unilateral iatrogenic keratectasia that developed 10 months after bilateral LASIK. This case involved enhancement surgery using a broad-beam excimer laser to treat -6.60 D of myopia. The ectasia progressed rapidly over a 12-month period.

Preoperative corneal thickness and depth of excimer laser ablation must be evaluated before LASIK to ensure that adequate posterior corneal stroma is preserved. Previous experience with lamellar surgery suggests that at least 250 µm of central posterior stromal tissue and more than half the original corneal thickness should be preserved to maintain long-term corneal integrity and avoid postoperative corneal steepening. If a 160-μm flap is created for LASIK, the average 550-μm cornea will have 140 µm of corneal stroma available for ablation.

Depending on the excimer laser, ablation zone size, and ablation nomogram used, the maximal LASIK correction for the average cornea ranges from 10.00 to 15.00 D. 58 Of course, the 250-μm posterior bed thickness that is recommended by many experts is merely an estimate. In rare cases, this may be insufficient.

There is a significant standard deviation in flap thickness obtained with all currently available microkeratomes. A more conservative approach is to assume the flap is 40 µm thicker than the average flap thickness obtained with the specific microkeratome that is being used. This may limit corrections in many patients to less than -8.00 D of myopia.

Anterior bulging of the posterior corneal surface has been correlated with residual corneal bed thickness using measurements performed with the Orbscan slit scanning corneal topography/pachymetry system. 59-63 This remains controversial, however, since the accuracy of these measurements has not been verified 64-65 and posterior ectasia is commonly noted with this instrument, even in thick corneas that underwent low corrections. 64,65 Many of these may be artifact. 64,65

Videokeratography is fundamental to the screening of candidates for refractive surgery. Appropriate preoperative detection and management of corneal topographic abnormalities are essential steps in every corneal refractive surgical procedure. A higher incidence of keratoconus has been reported in prospective refractive surgery patients than the general population, most likely due to self-selection. 6 Patients with irregular astigmatism caused by corneal ectasia do not achieve good vision with spectacles and tend to opt for rigid contact lenses or seek refractive surgery. It is important to identify these patients since they are more likely to have an unacceptable outcome.

**Dry Eye and LASIK-induced Neurotrophic Epitheliopathy**

Dry eye and other ocular surface disorders are frequent following LASIK. Lindstrom and colleagues 66 reported 3.4% incidence of dry eye after hyperopic LASIK.

Patients with mild to moderate dry eye frequently pursue refractive surgery because of increasing intolerance to contact lenses. Many of these patients are asymptomatic unless they are wearing contact lenses and most do well after LASIK. The health of the ocular surface should be optimized prior to surgery with non-preserved artificial tears and ointments. Consideration should be given to punctal occlusion for patients with persistent corneal rose bengal staining despite frequent artificial tears and bedtime ointments. Topical 0.05% cyclosporine treatment may be beneficial, but this medication is only available on a custom basis in the USA and the available formulations are not well tolerated. If Restasis (Allergan, Irvine, CA) is eventually approved, then this formulation may be much better tolerated and, therefore, more likely to improve the ocular surface prior to refractive surgery. Severe dry eye patients are not good candidates for LASIK. We have consulted on several of these patients with serious wound healing problems and persistent epithelial defects.

Many patients have dry eye symptoms for several months following LASIK. This is common even if the patient had no symptoms or signs of dry eye prior to surgery. Most of these patients have no signs of dry eye after LASIK either. Other patients develop mild to severe punctate epithelial erosions, punctate epithelial keratopathy, and rose bengal staining confined to the flap (Fig 9). We have found
that corneal rose bengal staining develops in approximately 2% of eyes that did not have this sign prior to LASIK (Wilson, unpublished data). Some investigators have suggested that tear production may be decreased following LASIK, but we have noted little difference in the Schirmer test without anesthesia between patients with corneal rose bengal staining and those without it at the same time points after surgery, if there was no dry eye prior to surgery. It makes physiological sense that LASIK would have little effect on tear production because only the central corneal nerves are severed. The peripheral corneal and conjunctival nerves that contribute to the ocular surface-central nervous system-lacrimal gland loop remain intact.

Our observations suggest that corneal surface abnormalities that develop after LASIK are attributable to LASIK-induced neurotrophic epitheliopathy due to temporary interruption of the corneal nerves during formation of the flap. The corneal epithelium is known to derive neurotrophic factors from the corneal nerves. Consider the corneal pathology that frequently develops in response to trigeminal neuropathy secondary to trauma or tumors or experimental denervation in the rabbit cornea. Evidence that the condition noted in LASIK patients is related to trigeminal denervation is, 1) development of the condition in many eyes with no signs or symptoms of dry eye prior to surgery, 2) changes are for the most part confined to the flap with the peripheral cornea being spared, 3) the area of the cornea around the hinge where nerve trunks are spared remains normal, 4) tear production monitored with the Schirmer test without anesthesia is relatively normal, and 5) the condition typically resolves approximately 6 to 8 months after LASIK. This corresponds well with the length of time required for regeneration of the nerves into the flap after LASIK.

Patients with signs of preexisting dry eye also develop LASIK-induced neurotrophic epitheliopathy. In fact, our experience is that they develop it more frequently and more severely than patients without dry eye prior to LASIK. Development of LASIK-induced neurotrophic epitheliopathy is suggested by marked worsening of corneal surface abnormalities in these dry eye patients.

Many patients with LASIK-induced neurotrophic epitheliopathy are asymptomatic since the central cornea is hypoesthetic for several months after the procedure. If, however, the ocular surface pathology affects the corneal epithelium overlying the entrance pupil, these patients may have frustrating fluctuating vision and decreased best corrected visual acuity that persist until the condition resolves.

Treatment of these patients is limited to frequent non-preserved artificial tears and ointments at bedtime. Some patients seem to benefit from punctal occlusion, even though they have normal tear levels. The main treatment for these patients is reassurance that the condition typically resolves by 6 to 8 months after surgery. If the eye has normal tear levels, then soft contact lenses may improve the visual problems by masking the surface abnormalities until the nerves regenerate. Contact lenses should not be used in eyes with low tear levels due
to the increased risk of microbial infection. We use a Schirmer test without anesthesia of 8 mm or more as an adequate level.

LASIK-induced neurotrophic epitheliopathy typically recurs with enhancement. We suggest enhancing one eye at a time when LASIK-induced neurotrophic epitheliopathy develops after primary LASIK.

Interestingly, patients who have PRK do not appear to develop a LASIK-induced neurotrophic epitheliopathy-like syndrome. This may be attributable to only the nerve endings being ablated. Therefore, nerves regenerate more quickly and the regenerating nerve endings are already in close proximity to the overlying corneal epithelium. For this reason, we consider PRK as an alternative to LASIK for patients with low myopia and mild or moderate dry eye prior to surgery.

**Diffuse Lamellar Keratitis**

Smith and Maloney thoroughly described diffuse lamellar keratitis (DLK) (American Academy of Ophthalmology, San Francisco, CA, November, 1997). Other reports have appeared since that time (Linebarger EJ. Diffuse lamellar keratitis: trouble in paradise? ASCRS Film Festival, Grand Prize Winner, 1999). It has also been called sands of the Sahara syndrome (Bobby Maddox, MD, El Paso, TX, coined the phrase), because of the characteristic wavy appearance at slit-lamp examination.

DLK is characterized by pain, photophobia, and reduced vision associated with diffuse non-infectious inflammation at the level of the interface during the first few days after LASIK (Fig 10). It may be multifocal in some cases. There is little or no anterior chamber reaction and the conjunctiva is relatively uninflamed. In severe cases, it is associated with stromal necrosis and irregular astigmatism.

Infection should always be considered in DLK. We suggest culture and initial treatment with fortified antibiotics (amikacin 20 mg/ml and vancomycin 50 mg/ml every hour) until infection has been ruled out, even if topical corticosteroids are also started at the time of diagnosis. Some surgeons feel that the specific diagnosis can be made based on the appearance at the slit lamp and, therefore, the toxicity of fortified antibiotics can be avoided. However, we have seen two cases of infectious keratitis in which treatment was inappropriately delayed because of erroneous diagnosis of DLK. Both cases had severe vision loss.

The incidence of DLK is highly variable. One report noted an incidence of approximately 1 in 500. Some high volume LASIK surgeons have reported never seeing a case in their own practice. We have seen only two mild cases in 3000 LASIK procedures. Others have experienced focal outbreaks of DLK that have included dozens of patients.

Grading systems have been proposed to distinguish the level of inflammation associated with DLK (Hatsis, American Society of Cataract and Refractive Surgery, San Diego, CA, April 1998). In
this system, DLK is graded from 1 (mild) to 4 (severe). Another grading system has been proposed by Linebarger (Linebarger, 1999, cited above).75

Stage 1 DLK is typically seen on day 1 postoperatively as white, granular cells in the periphery with sparing of the visual axis.

Stage 2 Typically seen on postoperative day 2 or 3, shows white cells in the visual axis.

Stage 3 DLK involves an aggregation of cells clumped in the visual axis and associated with haze and reduced vision.

Stage 4 Involves central stromal necrosis, melt, and secondary hyperopia with irregular astigmatism.

Grading systems of this type are subject to observer bias, but may be useful for communication among surgeons. Patients with mild cases (grade 1) typically have normal vision and little or no symptoms. At the other extreme, severe (grade 4) cases typically have decreased vision and severe pain associated with marked interface inflammation and necrosis that results in topographic flattening of the corneal contour, secondary irregular astigmatism, and poor vision.

Many potential etiologies for DLK have been proposed (Linebarger, 1999, cited above).75-77 Most of these are based on speculation without supporting data. These include betadine from surgical preps, impure balanced salt solution, retained meibomian secretions and other tear film components, metallic debris, use of improper detergents, t alc from gloves, thermal effects from the excimer laser, lubricants on the microkeratome or blades, topical medications such as anesthetics, bacterial cell wall hypersensitivity, and biofilms from inadequate sterilization protocols. The cause is likely multifactorial. The microkeratome or blade can be excluded in cases that occur following enhancement with lifting of the flap. Virtually all of these factors can be excluded in cases where DLK occurs following a simple epithelial defect in eyes that had prior LASIK.78

The bacterial cell wall hypersensitivity mechanism could have been the underlying factor in a recent epidemic of DLK.77 The authors suggested that the microkeratome or irrigating cannula became contaminated by bacteria. These bacteria may reside in water left standing in the sterilizer. If the contaminated instruments are cleaned and left to dry, bacteria could proliferate on residual trace protein and the bacterial cell count could increase significantly. If the instruments are then autoclaved prior to surgery, the bacteria will be killed, but heat stable lipopolysaccharides may be produced. The lipopolysaccharides are not detoxified by autoclaving. This hypothesis holds that lipopolysaccharides cause an inflammatory reaction that digest stromal collagen. Lipopolysaccharide is a highly variable polysaccharide chain covalently attached to lipid A. Lipid A is the toxic moiety of lipopolysaccharide.

Water should not be left standing in the basin in sterilizers. This promotes the growth of bacteria and could trigger DLK.77 Whether or not this is the true mechanism of DLK, it appears prudent to clean the instruments after each surgery day to clean the autodrape and water basin, rinse thoroughly with distilled water, completely dry the interior of the microkeratome and basin, and let the instrument stand dry. We recommend discussing appropriate care of the microkeratome with the manufacturer.

There is new experimental evidence for another endogenous mechanism for DLK. DLK has been noted after epithelial abrasions following LASIK.78 It has been noted in eyes following LASIK that subsequently developed epithelial ingrowth at the same site.20,35 This potential involvement of the corneal epithelium led to searches for a mechanism. A recent study (Hong, Lee, Liu, and Wilson, unpublished data, 2000) has demonstrated that interleukin-1 (IL-1) stimulates corneal fibroblasts to produce monocyte chemotactic and activating factor (MCAF) and other chemotactic factors. MCAF and these other cytokines attract monocytes. In the case of LASIK it seems that the interface would offer a path of least resistance for penetration of cells into the corneal stroma. Interleukin-1 is released from corneal epithelial cells in large amounts following cell injury or death. These data suggest that injury to the surface epithelium or epithelial debris left within the LASIK interface triggers production of factors that are chemotactic for inflammatory cells via interleukin-1 release. This mechanism could account for many DLK cases.

Surgical technique may limit DLK, whatever the underlying mechanism. Many high volume practices that have noted little DLK include interface irrigation after the ablation as a step in LASIK. This includes our own center where the interface is typically irrigated with 1 to 2 cc of 0.2-µm filtered BSS just prior to replacing the flap to its original position. This seems likely to decrease the concentration of any exogenous or endogenous factors that might be involved in the induction of DLK. In our experience, this irrigation does not increase the rate of flap displacement, perhaps because we routinely
A number of prominent surgeons do not use gloves during LASIK and do not report infection as a complication. Other surgeons prefer to wear surgical gloves. In the event of infection it would be difficult to defend not using gloves.

The augmented risk of bilateral simultaneous LASIK compared with sequential LASIK appears to be low. Nevertheless, it is important to inform the patient of the serious potential risk in the event that bilateral, simultaneous infection occurs. Bilateral surgery should probably not be performed on patients with a known history of impaired immunity. A bilateral microbial infection was reported in a human immunodeficiency virus-infected patient with no history of opportunistic infections and a T-helper lymphocyte count of 300 cells/mm³. Watanabe and colleagues also reported a case of bilateral staphylococcal bacterial keratitis after LASIK.

Infectious agents that have been reported after LASIK include virus, bacteria (including atypical mycobacteria and nocardia), fungus, and parasite (Al-Reefy M. Bacterial keratitis following laser in situ keratomileusis for hyperopia. J Refract Surg 1999;15(suppl):S216-S217). Culture-negative ulcerative keratitis has also been reported to occur after LASIK. These cases have been responsive to topical corticosteroids and may represent severe DLK. Infection must be ruled out in these rare cases.

One case of abscess with endophthalmitis has been reported. Corneal abscess, hypopyon, and an intense vitreous cellular reaction associated with endophthalmitis developed 3 days after uneventful astigmatic myopic LASIK. The patient was immediately given intravenous ciprofloxacin and topical vancomycin and ceftazidime. The hypopyon resolved 1 day after therapy was instituted. The infecting organism was Streptococcus pneumoniae. Best-corrected visual acuity 7 months later was 20/23 with a refractive error of -4.00 D. A stromal scar was believed to be responsible for the reduction in visual acuity.

If an infiltrate is noted, it should be treated as infectious until proven otherwise. Consultation with a cornea and external disease specialist is advised. Treatment must be aggressive because of the potential for rapid progression due to the interface extending across the cornea.

The deeper location of the typical microbial infection in LASIK makes it more difficult to obtain adequate access for culture and potentially decreases effective penetration of antimicrobial therapy. When infiltrates are noted within the stroma, it is recommended that the flap be lifted to obtain sufficient material for culture. This also allows antibiotics to
be applied directly to the interface. Cultures are critical and should include tests for bacteria, fungus, and acanthameoba. Acid-fast infection should be evaluated using the Ziehl-Nielson stain.

Fortified antibiotics (amikacin 20 mg/ml and vancomycin 50 mg/ml) should be applied every hour around the clock until the infection is controlled. These medications can be adjusted based on the results of culture and sensitivity testing. Some cases of lamellar interface infection following LASIK do not respond to surface application. It may be necessary to retract the flap with sutures to gain sufficient penetration of the antibiotics. Rarely, the flap may have to be removed if the infection cannot be controlled.

Fungal keratitis is a potentially devastating condition. It occurs most commonly following an injury involving vegetable matter. More than 60 species of fungi have been reported to cause keratomycosis, with the causative organism varying by geographic locale.97 We consulted on a case of fungal keratitis where there was delayed diagnosis resulting in the need for penetrating keratoplasty. Always obtain fungal cultures when microbial infection is suspected.

Candida and Aspergillus species are the most common fungal infections in the northern United States and Fusarium species are most common in the southern United States. Aspergillus appears to predominate internationally. In one series, topical amphotericin B was used when a diagnosis of Candida species infection was made; natamycin was used in non-candidal infections.96 Fungal keratitis can occur in the early postoperative period or several months after the LASIK procedure. Risk factors for the development of fungal keratitis include trauma and excessive topical corticosteroid use.90,91

Although nocardia keratitis is a rare condition, a high index of clinical suspicion should be maintained in agricultural workers or in patients with trauma who have patchy stromal infiltrates. Sulfonamides are the initial drug of choice, but gentamycin is an effective alternative. Nocardia keratitis responds well to medical treatment if it is diagnosed early.99

Pérez-Santonja and colleagues93 and Nascimento and colleagues100 described interface opacities in patients who had uncomplicated myopic keratomileusis. Nocardia asteroides keratitis was confirmed by microbiologic work-up and guided the correct treatment.

Several cases of non-tuberculous mycobacterial keratitis have been reported.87-89,101 Almost all of these opportunistic infections have occurred following accidental or surgical ocular trauma, usually associated with the use of local corticosteroids. Cultures and sensitivity testing are critical to determine appropriate treatment. Mycobacterium chelonae represents a rare and insidious cause of infection after LASIK. Diagnosis can be difficult and is often delayed. Mycobacterium keratitis complicating LASIK may be difficult to eradicate until the sequestered stromal infiltrate is drained. Rapid recognition of the causative organism and aggressive medical and surgical management of the infection, may improve the outcome. Reviglio and colleagues89 reported a case of Mycobacterium chelonae infection centrally on and under the flap 1 month after LASIK. This patient's condition did not improve with antibiotics, but responded to penetrating keratoplasty. Gelender and colleagues88 reported two cases of mycobacterium keratitis following LASIK. Topical fortified amikacin, daptomycin, tobramycin, and ciprofloxacin eventually controlled the infections. Topical prednisolone acetate and bandage contact lenses were used to control inflammation and pain. The infiltrates were slow to resolve. Eventually local necrosis eroded through the flaps. This was followed by rapid clearing of the infiltrates. Scarring of the cornea developed at the site of necrosis. Chung and colleagues87 reported a case of Mycobacterium chelonae keratitis after LASIK that was successfully treated with medical therapy and flap removal, along with intensive topical daptomycin 1% and Ocuflox (Allergan, Inc, Irvine, CA) over 5 weeks.

Ultraviolet exposure associated with excimer laser keratectomy appears to be an efficient trigger for the reactivation of latent HSV-1.102-107 Cases of herpetic keratitis have been reported after excimer laser surgery. We have effectively treated several patients with a remote history of herpes simplex keratitis. These patients were treated with acyclovir 200 mg five times a day beginning 3 days before surgery and continuing for 1 month after surgery. None of these patients developed breakthrough infections. Herpes simplex reactivation should always be considered in the differential diagnosis of patients with persistent corneal epithelial defects after refractive or therapeutic excimer procedures.108

Retinal Complications After LASIK

There is no evidence that LASIK triggers retinal complications. It has been hypothesized that the increase in intraocular pressure to levels greater
than 60 mmHg with the microkeratome ring 3 to 4 mm posterior to the limbus may exert traction at the vitreous base and trigger retinal breaks (Kim HM, Jung HR. Laser assisted in situ keratomileusis for high myopia. Ophthalmic Surg Lasers 1996;27:S508-S511). Eyes with high myopia are at risk for retinal detachment. With the large number of patients undergoing LASIK, there will be a timing correspondence between surgery and retinal detachment in some patients. For example, one study found that retinal detachment occurred in four (0.25%) of 1,554 eyes of four (0.45%) of 878 patients. In another study, Arevalo and colleagues reported on the vitreoretinal complications in 29,916 eyes that underwent LASIK. In that study, 14 eyes experienced rhegmatogenous retinal detachments, two eyes experienced corneoscleral perforations with the surgical microkeratome when a corneal flap was being performed (one experienced a vitreous hemorrhage and the other later experienced a rhegmatogenous retinal detachment), four eyes experienced retinal tears without rhegmatogenous retinal detachment, and one eye had a juxtafoveal choroidal neovascular membrane. The incidences reported in studies of LASIK patients are consistent with incidences reported in patients with myopia who have not had LASIK. Both of these complications are more common in high myopia in the absence of LASIK. Preoperative and postoperative fundus examinations are, however, important in the detection of complications and treatment at an early stage.

REFERENCES
LASIK Complications/Ambrósio and Wilson


LASIK Complications/Ambrósio and Wilson
