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LASIK Interface Complications: Etiology, Management, & Outcomes

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Abstract

The anatomy of the LASIK interface allows for a variety of potential complications to arise, unique etiologies with overlapping clinical presentations. Primary interface complications include infectious keratitis, diffuse lamellar keratitis (DLK), central toxic keratopathy (CTK), pressure-induced stromal keratopathy (PISK), and epithelial ingrowth. Infectious keratitis is most commonly caused by Methicill in resistant *S. aureus* (early onset) or atypical Mycobacterium (late onset) postoperatively, and immediate treatment includes flap lift and irrigation, cultures, and initiation of broad-spectrum topical antibiotics, with possible flap amputation for recalcitrant cases. DLK is a white blood cell infiltrate that appears within the first 5 days postoperatively and is acutely responsive to aggressive topical and oral steroid use in the early stages but may require flap lift and irrigation to prevent flap necrosis if inflammation worsens. In contrast, PISK is caused by acute steroid response and resolves only with cessation of steroid use and IOP lowering. Without appropriate therapy PISK can result in severe optic nerve damage. CTK mimics stage 4 DLK but occurs early in the postoperative period is non-inflammatory. Observation is the only effective treatment, and flap lift is usually not warranted. Epithelial ingrowth is easily distinguishable from other interface complications and may be self-limited or require flap lift to treat irregular astigmatism and prevent flap melt. Differentiating between interface entities is critical to rapid appropriate diagnosis, treatment, and ultimate visual outcome. While initial presentations may overlap significantly, the conditions can be readily distinguished with close follow-up and most complications can resolve without significant visual sequelae when treated appropriately.

With the advent of keratomileusis procedures, primarily laser in situ keratomileusis (LASIK), a new anatomic region in the cornea came into existence: the potential space between anterior and posterior corneal lamellae commonly referred to as the LASIK interface. Within this region a number of biochemical processes occur after creation of the corneal flap, including limited wound healing and intercellular reorganization.¹ The anatomy of the LASIK interface allows for a variety of potential unique complications to arise from different etiologies with often overlapping clinical presentations.

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Primary interface complications include infectious keratitis, diffuse lamellar keratitis (DLK), pressure-induced stromal keratopathy (PISK), central toxic keratopathy (CTK), and epithelial ingrowth. Clarifying the nomenclature used for each entity is critical to enhancing future communication, and we propose the preceding terms be used. Benign interface debris may also be present in the interface, and while this does not routinely cause any problems, it may be confused with more serious disorders, resulting in inappropriate diagnoses and treatments. While some of these entities originate specifically within the interface, others may originate elsewhere but ultimately coalesce in this potential space.

Differentiating between interface entities rapidly is critical to appropriate diagnosis, treatment, and ultimate visual outcome. While initial similarities exist, taking a careful history of symptoms, timing, and onset, combined with a focused clinical exam, significantly improves the potential for accurate initial diagnosis and treatment protocol at presentation. In cases with significant overlap, continued close and frequent follow-up in the early postoperative period will allow for accurate diagnosis and potential modifications in treatment protocol when necessary.

Among interface complications, infectious keratitis is usually the most sight threatening, while DLK is both the most common to present and the most common etiology mistaken for other conditions, including infections, CTK, and PISK. Epithelial ingrowth is generally the easiest entity to identify and treat, although it may occasionally be associated with other interface disorders.

Each of these entities is relatively rare, occurring approximately in less than 1/500–1/1000 eyes in aggregate in the absence of outbreaks.^{2, 3} This rarity makes the initial diagnosis increasingly challenging for less experienced surgeons and clinicians. The goal of this review is to define the nomenclature and describe the etiology, diagnostic criteria, and optimal management strategies for these primary LASIK interface complications.

Literature Search Methodology

The search engine PubMed (www.pubmed.org) was utilized for literature search. The following search terms were used both in isolation and a variety of combinations: LASIK Interface, LASIK Infection, DLK & “diffuse lamellar keratitis”, LASIK keratitis, PISK and “pressure induced stromal keratitis”, CTK and “central toxic keratopathy”, and epithelial ingrowth. The articles reviewed were restricted to studies published in English, and animal studies were only included if they elucidated specific mechanisms for the complications reviewed. The searches were then reviewed by title for relevance. Among included citations, the reference list for each was also examined for relevant articles. While, at a minimum, the abstracts of all related articles were reviewed, only the articles deemed most relevant and current to this review topic were included. The references included in this review are therefore not all-inclusive; rather, they represent the majority of major citations, regardless of publication date, and the majority of the most recent references on the topics covered in this review.

LASIK Interface Complications: Overview

While each of these entities may belong in the initial differential of patients presenting with symptoms and interface findings, most can be quickly differentiated based on key historical elements, such as time of onset after surgery, level of discomfort (or lack thereof), as well as a thorough physical examination, including intraocular pressure (IOP) measurements [Table 1]. Interface complications can have a focal or diffuse appearance, present with or without conjunctival erythema, with or without foreign body sensation, and may present from 1 day to 3–4 weeks postoperatively [Table 1]. It is important to determine the specific etiology rapidly, because appropriate interventions are quite different depending on etiology, and in some instances may be exactly opposite [Table 2]. Interface complications evolve in appearance over time [Table 3]. A photographic array provides the classic appearance for each condition (Figures 1–6). Unfortunately, many of these entities may overlap in initial clinical appearance.

Infectious Keratitis

Etiology

Infectious keratitis is a rare but potentially devastating complication after LASIK.^{2, 4–13} Table 4 provides an overview from the largest studies to date on infectious keratitis after LASIK. A variety of organisms are implicated, including viruses (esp. Adenovirus and HSV), bacteria (esp. *Staphylococcus* and *Pseudomonas* species), atypical mycobacteria, Fungi, and acanthamoeba.^{2, 4, 8, 9} Adenovirus usually has a relatively benign course with ultimately good acuity, while HSV frequently leads to loss of best acuity after PRK or LASIK and is a relative contraindication for excimer laser surgery.⁸

The most common non-viral cause of infectious keratitis has evolved over time: prior to 2005, atypical *Mycobacterium* was the most common infectious etiology after LASIK,^{4, 6, 7} while recently gram-positive organisms, particularly Methicillin resistant *S. aureus* (MRSA), have become more common in the early postoperative period.^{2, 8, 10} *Strep* sp., *pseudomonas* sp., fungal infections, and acanthamoeba are less common organisms.^{2, 4, 8, 9} The reduced incidence of atypical *Mycobacterium* has been attributed to the routine use of fourth generation fluoroquinolones, which are more effective against these species.^{8, 14, 15} Concurrently, MRSA incidence may be increasing due to the potential for these species to develop concurrent resistance to fluoroquinolones.¹⁶

Risk factors for the development of infectious keratitis include blepharitis, dry eye, intraoperative epithelial defects, intraoperative contamination, delayed postoperative reepithelialization of the cornea, use of topical corticosteroids, and patients in the health profession.^{2, 4, 7} Preoperatively, the lids and lacrimal apparatus should be examined thoroughly, and appropriate treatment of lid disease should be undertaken.⁵ Furthermore, several epidemics of atypical mycobacteria have been associated with the use of non-sterile water to clean instruments or the use of ice during LASIK.⁶

Infectious keratitis after LASIK has been divided into infections occurring within the first 2 weeks (early onset) and after 2 week to 3 months (late onset).⁵ The organisms responsible

for early onset infections include staphylococcal and streptococcal species, whereas organisms more commonly seen in late onset infections include atypical mycobacteria, and fungi.

Management

In the initial phase of treatment, LASIK flaps should be lifted, cultures taken, the flap bed irrigated with fortified antibiotics, and broad-spectrum topical antibiotics started [Table 2]. For infections with a delayed onset, the use of amikacin may be beneficial in treating atypical mycobacteria.⁵ In no n-responsive LASIK infections, flap amputation may be necessary to facilitate antibiotic penetration.⁵

Outcomes

Most infections resolve with mild to moderate loss of best visual acuity,¹³ but rarely therapeutic penetrating keratoplasty is necessary [Figure 7].

Diffuse Lamellar Keratitis (DLK)

Etiology

Diffuse lamellar keratitis (DLK) is a white blood cell infiltrate that coalesces between the flap and stromal bed that appears within a few days (1–5) after laser in-situ keratomileusis (Figure 2).^{3, 17, 18} Confocal microscopy has confirmed the presence of inflammatory cells in the corneal stroma and interface.¹⁹ This non-specific interface inflammation is certainly associated with intraoperative epithelial defects,²⁰ and has been linked to multiple rare potential inciting factors.²¹ However, the majority of cases, especially DLK epidemics, can be linked to bacterial endotoxins, especially in sterilization reservoirs^{3, 22–26} or issues during the instrument sterilization process.^{27, 28} Isolated idiopathic DLK cases occur sporadically,²⁹ however, if more than one case occurs in a short time, steps should be undertaken to evaluate the sterilization process.^{3, 22, 23} Late onset DLK has also been described in literature^{30, 31}; however, most of these cases are likely due to some specific causative factor.

DLK is typically classified clinically in to 4 stages as described by Linebarger and colleagues.³² Stage 1 has inflammatory cells in the far periphery only, which are first present in the corneal stroma and then coalesce in the LASIK interface. Stage 2 has a diffuse infiltrate frequently involving the paracentral and peripheral flap margins but sparing the central axis. Stage 3 has a denser infiltrate within the flap interface, which involves the visual axis and is frequently associated with decreased visual acuity. Stage 4 has a focal, coalesced dense haze with scarring, signifying flap necrosis and usually results in permanent corneal scarring, with visual acuity loss of varying severity (Figure 8). DLK appears to be slightly more common when the femtosecond laser is used for flap creation^{33–35}; however, most of these cases appear to be mild and resolve with minimal treatment.

Management

DLK is highly sensitive to steroids and responsive to aggressive topical steroids for mild cases, frequently up to every hour administration, and a combination of topical and oral

steroids in moderate cases.^{3, 36, 37} Many surgeons advocate using oral steroids for stage 2 and 3 DLK, with flap lift and irrigation for stage 2 cases that are not responding rapidly to treatment and all stage 3 cases.^{3, 36, 37} For Stage 4, aggressive steroids to minimize scar density are warranted and may be partially effective.^{32, 36} Flap lift for stage 4 is more controversial, with some surgeons advocating cautious flap lift and irrigation to remove inciting toxins, but extreme care must be taken to prevent tissue loss; therefore some advocate no flap lift for stage 4 cases.³²

Outcomes

Reported uncorrected and corrected visual acuity after DLK resolves is generally quite good [Table 5].^{3, 18, 22, 29, 38} However, this may be misleading, as DLK appears to affect visual quality and contrast sensitivity more than absolute Snellen acuity measurements.³⁸ DLK frequently induces a mild to moderate hyperopic shift after resolution, with potentially both regular and irregular astigmatism, especially in stage 4 cases.^{18, 38} Enhancement rates are higher in patients that develop DLK.^{3, 29, 38} If significant ametropia persists, patients may undergo retreatment without increased risk of developing DLK a second time as long as the inciting issue has been resolved, such as elimination of endotoxin in sterilization units. For stage 4 cases, retreatment may still be warranted if the refractive error is not irregular, but in these cases surface ablation is often a better option than flap lift for the aforementioned reasons.

Pressure-Induced Stromal Keratopathy (PISK)

Etiology

In the setting of LASIK, PISK is a relatively rapid steroid response resulting in high intraocular pressure with resulting fluid accumulation in the interface. The amount of fluid present may be relatively small, resulting in diffuse haziness in the interface and overlying stroma without an obvious fluid layer³⁹ [Figure 4], or it may be pronounced [Figure 9], resulting in a visible fluid cleft separating the anterior flap from the posterior residual bed.⁴⁰ PISK appears to be a more complex entity to identify than other interface complications due to confusing nomenclature in the literature and to the wide variety of appearances and findings on presentation.

Nomenclature

Multiple names have been given to the various manifestations of this entity, potentially resulting in confusion and misleading diagnostic criteria. Among the most common terms are pressure-induced stromal *keratitis* (PISK),³⁹ pressure-induced interface *keratitis*,⁴¹ and interface fluid syndrome (IFS).^{42, 43} “Keratitis” is a misnomer in this condition, as confocal evaluations have demonstrated that no actual keratocyte inflammation is present.^{44, 45} Interface fluid syndrome (IFS) is technically correct; however, IFS may occur from a variety of different mechanisms unrelated to acute steroid response in the early postoperative period, and to many clinicians the term implies that interface fluid that is readily visible. Therefore, while correct, we recommend against the routine use of IFS to communicate information about this specific entity occurring in the early postoperative period after LASIK associated with steroid use and presenting with or without obvious interface fluid.

Recently, Tourtas and Cursiefen⁴⁶ coined the term “pressure induced stromal *keratopathy* (PISK),” which maintains the most common abbreviated term “PISK” while also accurately and most effectively communicating the etiology of the condition. We therefore recommend this term be adopted moving forward and will use it throughout this review.

Management

While PISK has been described in detail,^{39–45, 47–50} the significant variability in clinical presentation, from diffuse haze to demonstrable interface fluid, requires added diligence in establishing the diagnosis, differentiating this condition from diffuse lamellar keratitis (DLK), and initiating an appropriate treatment strategy. The degree of interface fluid accumulation masks true IOP in various ways when measured using standard approaches. In all cases, actual IOP is greater than IOP measured centrally, and peripheral measurements generate a more accurate IOP. With small amounts of fluid, IOP measurements may be elevated but still falsely low, while with larger fluid clefts IOP will measure extremely low due to the cushioning effect of the interface fluid.

For any patient on chronic steroids after LASIK (two weeks or longer), it is critical to routinely measure IOP, even in the early postoperative period. IOP measurement, especially when obtained centrally, is artifactually reduced in a predictable way after routine LASIK⁵¹; therefore, any increased IOP postoperatively warrants further investigation. Whenever IOP measurements are suspect, alternative means should be attempted to determine IOP, including peripheral IOP measurements with Goldmann applanation or tonopen.^{52–54} Dynamic contour tonometry may also be employed to assess true IOP, as it has been shown to be relatively immune to changes in corneal biomechanics and pachymetry after LASIK.⁵⁵ Appropriate management includes cessation of steroid use and initiating topical anti-glaucoma medications until the fluid resolves.^{39–41, 43, 47, 48, 50}

Outcomes

Severe glaucomatous field loss and decreased central visual acuity can occur if PISK is not recognized early and managed appropriately.^{40, 41, 47, 49} If identified and appropriately managed early, typically patients do well without loss of BCVA.^{39, 50}

Central Toxic Keratopathy (CTK)

Etiology

CTK is a rare, acute, non-inflammatory central corneal opacification that can occur within days after uneventful LASIK or PRK (Figure 5).^{56–62} Etiology is unknown but may be related to enzymatic degradation of keratocytes.^{57, 60} Confocal microscopy has demonstrated activated keratocytes without inflammatory cells, with initial keratocyte loss from the stromal bed, with gradual repopulation over time.^{63, 64} CTK has been reported to demonstrate anterior curvature flattening without alteration of posterior curvature in anterior segment tomography⁶⁵; however, some cases do appear to alter all tomographic findings, likely as measurement artifact [Figure 10]. The onset is acute without worsening over time, as opposed to most other interface entities.

Management

The first critical step in appropriate management is distinguishing CTK from stage 4 DLK.⁵⁸ CTK is almost always painless, as opposed to DLK, which in almost all cases has at least a moderate foreign body sensation, and CTK is acute in onset, as opposed to the progression over time to stage 4 DLK. CTK is self-limited and treatment is not warranted.⁵⁷ While some have advocated aggressive topical steroid use⁶¹ or flap lift and irrigation,⁶⁶ most feel that surgical intervention will not help and may worsen the final outcome.^{56, 57, 60}

Outcomes

Most individuals nearly fully recover after a variable, often protracted clinical course; however, most patients retain some faint corneal haze, and some have a visually significant, persistent hyperopic shift.^{57, 60, 65}

Epithelial Ingrowth

Etiology

Epithelial ingrowth at the far periphery is a normal healing response to LASIK flap creation,¹ but clinically-relevant epithelial ingrowth occurs when a fistula develops under the flap allowing epithelial cell growth into the interface.⁶⁷ Most cases can be observed without requiring intervention.⁶⁷ With femtosecond laser flap creation, the overall incidence of visually significant epithelial ingrowth has decreased.⁶⁸ In some eyes, epithelial ingrowth may require treatment for a variety of reasons listed in Table 8 [Figure 11].^{67, 69} For primary LASIK, increased epithelial ingrowth incidence is associated with mechanical microkeratomes as compared to femtosecond lasers for flap creation,³³ hyperopic LASIK treatment,⁷⁰ LASIK after RK,⁷¹ epithelial defects during surgery,⁷² and older age.⁷³ For LASIK retreatment, increased epithelial ingrowth incidence is associated with the use of contact lenses after retreatment⁷³ and flap-lift retreatment performed 3 or more years after primary LASIK.⁷⁴

Management

Treatment depends on the clinical situation. Majority of cases of mild, clinically insignificant ingrowth are managed with observation. Initial surgical treatment for epithelial ingrowth is performed with flap lift, removal of epithelial cells from the posterior surface of the flap and the stromal bed with a blade or similar instrument, and replacement of the flap without sutures or tissue glue.^{67, 75} With recurrent episodes of epithelial ingrowth, additional measures are typically taken, including flap suture,^{76, 77} fibrin glue,^{78, 79} or YAG laser treatment.⁸⁰

Outcomes

As long as flap melt does not occur, patients typically retain UDVA and CDVA following appropriate management with low rates of recurrence.

Distinguishing between Various Interface Complications

The key to appropriate management of LASIK interface disorders is distinguishing them from one another. Epithelial ingrowth has a highly characteristic appearance and is therefore rarely mistaken for any other condition; however, the other four entities may have overlapping presentations. In addition to presenting symptoms and appearance [Table 1], timing of onset is important in distinguishing between various entities [Figure 12].

Distinguishing Infectious Keratitis from other possible etiologies

The appearance of a focal infiltrate at any time point, or a new infiltrate of any configuration more than one week after LASIK, should be presumed infectious until proven otherwise. Infectious etiologies are most commonly symptomatic, accompanied by increased foreign body sensation and some degree of visual reduction, with significantly increased conjunctival erythema, which is unique among interface disorders [Table 1]. The infiltrate is focal in nature with surrounding inflammatory cells with haze, as opposed to the more diffuse appearance of DLK. Unlike DLK, the inflammation associated infectious keratitis persists despite topical corticosteroid use. Infectious keratitis is dissimilar from PISK or CTK.

Distinguishing DLK from other possible etiologies

At various times in its clinical course, DLK may mimic benign interface debris (DLK Stage 1–2) [Figures 1 & 2], PISK (DLK Stage 3) [Figure 4], and CTK (DLK Stage 4) [Figure 5], and has been confused with infectious etiologies at various stages. The prominent element of DLK is early onset, evolution in appearance over time, and dramatic response to steroids; these features should facilitate distinguishing DLK from all other interface entities.

Benign interface debris is asymptomatic and does not change over time, with or without steroid use. PISK takes at least 2 weeks to develop, as compared to the early onset of DLK, and does not improve with steroid use.^{39–41, 50} All patients with the presumptive diagnosis of DLK managed on aggressive steroids should have that diagnosis reconsidered if there is no dramatic change in clinical appearance within 2 weeks. IOP measurement is critical when steroids are used for more than one week after LASIK. CTK is painless, presents almost immediately with a stage 4 DLK-like appearance within the first few days after surgery, and does not evolve over time, as opposed to DLK, which takes longer to evolve to this appearance.

Summary

A variety of complications can present in the LASIK interface, with overlapping clinical features but unique mechanisms, time courses, and management strategies. Differentiating between these interface disorders by taking a careful history of symptoms and onset, combined with a focused clinical exam, allows for accurate diagnosis and treatment on presentation. Close attention to these specific features should lead the clinician rapidly to the appropriate diagnosis and optimal management.

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Figure 1. Benign interface debris in the LASIK interface. (Reprinted from Randleman JB. Chapter 8: Etiology and clinical presentations of irregular astigmatism after keratorefractive surgery. In: Wang M, ed. *Irregular Astigmatism: Diagnosis and Treatment*. SLACK Inc., Thorofare, NJ 2007: 79–90)

Figure 2. Infectious keratitis. Note the focal infiltrates interspersed within the somewhat diffuse inflammatory reaction. The causative organism was *Mycobacteria*.

Figure 3.
Diffuse lamellar keratitis (DLK), stage 3. Note the diffuse, granular haze throughout the central cornea.

Figure 4. Pressure induced stromal keratopathy (PISK) with a diffuse, hazy interface but without an obvious fluid layer. (Image courtesy of Theofilos Tourtas, M.D.)

Figure 5. Central toxic keratopathy (CTK). Note the focal corneal haze with a striate appearance within the center of the haze. (Image courtesy of Joung Y. Kim, M.D.)

Figure 6.
Epithelial ingrowth, with a nest of epithelial cells notable extending in from the 7 o'clock meridian.

Figure 7.

Infectious keratitis. The infection that began in the interface has now extended through the flap anteriorly and posteriorly to become a full-thickness infiltrate with a hypopyon. This cornea perforated the following day, requiring penetrating keratoplasty.

Figure 8.

DLK, Stage 4. A) Note the focal corneal haze with a striate appearance within the center of the haze similar to the appearance of CTK. B) Corresponding topography with notable focal flattening corresponding to the focal haze. (Reprinted from Randleman JB. Chapter 8: Etiology and clinical presentations of irregular astigmatism after keratorefractive surgery. In: Wang M, ed. *Irregular Astigmatism: Diagnosis and Treatment*. SLACK Inc., Thorofare, NJ 2007: 79–90)

Figure 9.
PISK with an obvious fluid cleft. (Image courtesy of Marc Michelson, M.D. and Matthew J. Fabrizio, M.D.)

OCULUS - PENTACAM

OCULUS - PENTACAM

Belin / Ambrosio Enhanced Ectasia

Figure 10.

Pentacam image of central toxic keratopathy, demonstrating significant focal flattening noted in sagittal curvature map corresponding to focal corneal haze. Note that the corneal thickness (A) and posterior elevation maps (A&B) are also significantly focally altered, likely due to measurement artifact. These changes resolved over time (not shown).

Figure 11.

A) Focal area of epithelial ingrowth noted on slit lamp exam with B) corresponding focal irregular astigmatism noted on topography. (Reprinted from Randleman JB. Chapter 8: Etiology and clinical presentations of irregular astigmatism after keratorefractive surgery. In: Wang M, ed. *Irregular Astigmatism: Diagnosis and Treatment*. SLACK Inc., Thorofare, NJ 2007: 79–90)

Figure 12.

Schematic representation of relative onset and severity of the overlapping interface complications. The Y-axis represents that time point by which that relative percentage of cases usually present and the relative severity of each complication; the decline in percentage on the Y-axis for DLK indicates the likelihood that DLK should begin to evolve and resolve with appropriate management over that time course.

Table 1

LASIK Interface Disorders: Characteristics

Clinical parameters	DLK	CTK	PISK	Infection	Epithelia I Ingrowth
Etiology	Inflammatory	Toxic	Fluid (steroid response)	Bacteria Mycobacterium Fungi	Epithelial cells in interface
Typical Onset	1–5 days	2–7 days	10–21 days	3–21 days	14 days or later
Initial effect on visual acuity	Minimal	Pronounced	Pronounced	Variable	Minimal
Pain	Foreign Body sensation	None	Minimal	Moderate	None
Location	Diffuse	Focal, well defined	Diffuse	Focal, less defined	At flap edge
Corneal Haze	Granular until stage 4	Dense focally, clear surrounding	Diffuse haze	Dense at infiltrate, variable surrounding	Focal at cells
Conjunctival erythema	None	None	None	Moderate to severe	None
IOP (measured)	Normal	Normal	Normal or low	Normal	Normal
IOP (real)	Normal	Normal	High	Normal	Normal
Interface Fluid	None	None	Yes (may not be apparent)	None	None
Response to Topical Steroids	Minimal/good	Minimal/none	Poor with worsening	Variable	None
Response to Oral Steroids	Good/excellent	Minimal/none	None/mild worsening	Limited	None
Response to Flap lift	Good	Poor	None	Good, depending on flap integrity	Good, may require flap sutures

DLK = Diffuse lamellar keratitis

CTK = Central Toxic Keratopathy

PISK = Pressure-induced stromal keratopathy

Table 2

LASIK Interface Disorders Management

Etiology	Primary Intervention	Secondary Intervention	<i>Contraindicated Management Strategies</i>
Infectious Keratitis	Topical Antibiotics, Flap lift/Irrigate/Culture	Flap Amputation if unresponsive	<i>Steroid use without antibiotics</i>
DLK	Steroids (Topical & Oral)	Flap Lift & irrigate	<i>Failure to use steroids</i>
PISK	Steroid Cessation	IOP lowering Medications	<i>Continued Steroid use</i>
CTK	Observation	Observation	<i>Flap lift</i>
Epithelial Ingrowth	Observation if only at flap edge	Flap lift/cell removal/flap suture	<i>N/A</i>

DLK = Diffuse lamellar keratitis

PISK = Pressure-induced stromal keratopathy

CTK = Central Toxic Keratopathy

Table 3

Signs & Symptoms of Interface Disorders Over Time

Day	DLK	CTK	PISK	Infectious
1	FBS ± peripheral infiltrate (I)	None	None	Extremely Rare
2–3	Increased infiltrate (II)	Dense central opacification	None	Rarely
4–7	More dense infiltrate, coalescing (II–III)	Stable opacification	None	FBS, conjunctival hyperemia, Infiltrate (bacterial)
8–14	Coalescence to focal opacity ± scarring (III–IV)	Stable	None	Worsening of symptoms (bacterial) Onset of symptoms (fungal)
15–21	Final coalescence to stage IV or resolution	Stable	Onset of haze	Worsening (bacterial, fungal) Onset (mycobacterial)
22–35	Final outcome	Slow resolution	Worsening haze ± fluid cleft	Variable depending on organism and treatment

DLK = Diffuse lamellar keratitis

CTK = Central Toxic Keratopathy

PISK = Pressure-induced stromal keratopathy

WBC = white blood cells

FBS = foreign body sensation

I–IV = stages of DLK

Table 4

Overview of Infectious Keratitis after LASIK

Study	Year	Total eyes	Total Infections (eyes)	Incidence	# Culture positive	Primary Organism	Final CDVA > 20/20	Final CDVA > 20/40
Karp ⁵	2003	N/A	15	N/A	15	<i>Mycobacterium</i> (6) <i>S. aureus</i> (4) <i>Pseudomonas</i> (1) Fungal (3) Acanthamoeba (1)	5/15 (33%)	10/15 (66%) NLP: 2 (13%)
Freitis ⁴	2003	N/A	10	N/A	N/A	<i>Mycobacterium</i> (10)	0 (0%)	4 (40%)
Solomon ⁸	2003	338,500 [*]	116	0.03% [*]	46/69 (66%)	<i>Mycobacterium</i> (33) <i>Staph</i> sp. (23) <i>Strep</i> sp. (2) Gram negative (2) Fungal (7) <i>Nocardia</i> (2)	^37/69 (53%)	^58 (84%)
Moshifar ⁷	2007	10,477	33	0.31%	23 cases (viral) 10/33 cases (bacterial)	Adenovirus (18) HSV (5) <i>Mycobacterium</i> (4) <i>Staph</i> sp. (3) <i>Pseudomonas</i> (1) Polymicrobial (2)	20/33 (59%)	26/33 (77%)
Solomon ⁹	2007	N/A	10 (LASIK)	N/A	N/A	MRSA (100%)	1 (10%)	8 (80%)
Llove ⁶	2010	204,586	72	0.035%	21/54 (39%)	<i>S. epidermidis</i> (9) <i>S. pneumoniae</i> (8) <i>S. viridans</i> (2) <i>S. pyogenes</i> (1) <i>S. aureus</i> (1)	38/72 (53%)	67/72 (93%)
Garg ¹⁰	2010	N/A	17	N/A	N/A	<i>Nocardia</i> (5) <i>Mycobacterium</i> (4) Fungal (4) Acanthamoeba (2) <i>Corynebacterium</i> (1) <i>S. epidermidis</i> (1)	1 (6%)	4 (24%) CF or worse: 8 (47%)
Yamaguchi ¹¹	2011	N/A	39	N/A	11/30 (36%)	<i>Mycobacterium</i> (9) <i>Corynebacterium</i> (1) Gram + (1)	22 (56%)	33 (85%)

* : the total number of cases in So Iomon et al. was estimated based on survey responses

^ : % 20/20 and 20/40 were derived from culture-positive cases only

Table 5

Diffuse lamellar Keratitis (DLK) Incidence, Outcomes, and Associations

Study	Year	# Eyes Studied	Incidence	CDVA Outcomes	UDVA Outcomes	Association
Holland ¹⁹	2000	983	52 (5.3%)	98.1% 20/30	Not reported	Endotoxins released from gram-negative biofilms in sterilizer reservoirs
Johnson ¹⁶	2001	2,711	36 (1.3%)	66.6% 20/20 88.8% 20/25	27.7% 20/20 47.2% 20/25	Overlying epithelial defects
Wilson ²⁶	2002	1,352 primary 217 enhancements	17 (0.9%) 3 (1.4%)	100% 20/30 (primary) 100% 20/30 (enhancement)	Not reported	Multifactorial endogenous factors
Stulting ¹⁵	2004	15,119	61 (0.40%)	81.3% 20/20 96.6% 20/25	55.9% 20/20 72.8% 20/25	Endotoxin (Cassette autoclave with reservoir) (47 eyes- 0.94%)
Javaloy ^{20, 29}	2011	1,161	209 (18%)	76.5% 20/20 91.4% 20/25	54.5% 20/20 75.2% 20/25	*Endotoxin (Cassette autoclave with reservoir) *Multifactorial Causes

Table 6

Pressure Induces Stromal Keratopathy (PISK)

Study	Year	Term Used	# Patients	Age Range	IOP range (mmHg)	Method	Interface fluid	Time to diagnosis	VF loss	Visual Outcomes
Belin ³⁰	2002	Pressure induced stromal keratitis	4 (7 eyes)	33-48	27-38	PN	No	13 days - 4 months	Not reported	UDVA: 14.3% 20/20 57.1% 20/25
Hamilton ³⁹	2002	Interface fluid	4 (6 eyes)	19-58	30-57	TP	Yes - 4 eyes	<4 weeks - 6 months	4 (marked visual field loss in 1 case)	CDVA: LP (1 eye) 20/400 (2 eyes) 3 eyes 20/50
Nordlund ³¹	2004	Pressure induced interface keratitis	6 (10 eyes)	28-55	32-42	Not reported	No	1 week - 9 weeks	Not reported	CDVA: 80% 20/20 90% 20/30
Galal ³⁸	2006	Steroid induced elevation of intraocular pressure	8 (13 eyes)	31.4±5.3* (mean)	24-56*	GAT	Yes - 2 eyes	2 weeks - 3 months	2 eyes	UDVA: (logMAR) 0.9±0.18*

PN: Pneumatonometer

TN: Tono-pen

GAT: Goldmann Applanation Tonometry

VF = visual field

* : Results reported include patients in Group 1: misdiagnosed initially as DLK

Table 7

Central Toxic Keratopathy (CTK)

Study	Year	# Cases after LASIK	Time to presentation (days)	Time to resolution (months)	Final CDVA > 20/20	Final CDVA > 20/40
Sonmez ⁴⁷	2007	19 eyes	3–9	2–18	16 (84%)	18 (95%)
Hainline ⁵⁰	2007	9 eyes	5–10	1–4	4 (44%)	9 (100%)

Table 8

Reasons for Intervention for Epithelial Ingrowth

Finding	Symptom
Extension into visual axis	Decreased acuity
Extension to edge of pupil	Increased glare
Focal flap elevation (paracentral)	Induced irregular astigmatism
Focal flap elevation (flap edge)	Foreign body sensation
Induced keratolysis	Focal flap melt