Special Article

A Mysterious Tale: The Search for the Cause of 100+ Cases of Diffuse Lamellar Keratitis

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Three years ago I began developing a refractive surgery practice. Training was accomplished, a LASIK suite was constructed, a broad beam laser was purchased, a heating/ventilating/air conditioning (HVAC) system with HEPA filter was installed, and we were ready to go. Little did I realize the troubles to come.

Money evaporated like water as huge sums of advertising dollars were spent on radio, cable TV, and newsprint advertising to get the ball rolling. Initial surgery went well, but diffuse lamellar keratitis (DLK) was experienced in 20% of cases. Furthermore, this rate of DLK increased over time to as much as 50% of eyes with this postoperative inflammatory response. Over the next 2 years, a myriad of corrective measures were tried, and I became an unwitting expert on the treatment of DLK. Uninterrupted weekends became a thing of the past, as I would be in the office every Saturday and Sunday monitoring the course of Sands of the Sahara patients. Surgery to lift flaps for irrigation to control DLK frequently interrupted both the daily office routine as well as weekend activities. Healing was slow, but anxiety was high for patients and physician. Ultimately, most patients did well, but epithelial ingrowth, irregular astigmatism, loss of BSCVA, and consecutive hyperopia all have occurred, and required a variety of treatment modalities to improve if not to completely remediate these problems. Throughout this odyssey, phone calls and frequent rechecks of patients in actual trouble or severe states of anxiety have managed to carry the day until this nightmare could be initially ameliorated, and then ultimately eliminated from an otherwise relatively complication-free ophthalmology practice.

In searching for an answer to this puzzle, several facts were noted. DLK occurred bilaterally more often than unilaterally. In the unilateral cases there was no preference for one eye over the other. Surgery performed early in the day versus later in the day seemed to make no difference. Sands of the Sahara would occur with simple flap relifting for enhancement as well as with de novo surgery.

Looking for answers at LASIK meetings and visiting other LASIK facilities was not helpful. Our level of caution far exceeded those facilities we visited, yet they had no Sands occurrences. A phone call to the state environmental control lab looking for answers was rather discouraging. I was told that not knowing what we were looking for would make the investigation terribly difficult—like looking for a needle in a haystack. It would probably not be worthwhile and would be quite expensive. An outside consultant reviewed our procedures and could only add that the shoe covers, which we wore, should be donned just before entering the LASIK suite rather than applying them on the second floor and then walking to the third floor LASIK suite. This would avoid tracking in any rug fibers. Other than that, he had no suggestions, and was as perplexed as we were about the cause of this DLK scenario.

A list of all efforts sequentially employed to eliminate DLK follows, along with the rationale for each endeavor is presented in Table 1.

The air quality analysis referenced in Table 1, #28, was conducted during a day of actual LASIK surgery. First, the consultants obtained baseline levels of suspended air particles throughout the building. Surprisingly, the particle counts in the LASIK suite were about half of that in unfiltered portions of the building (Table 2). With HEPA filtration, one should expect dramatically lower particle counts in the LASIK facility. Subsequently during surgery it was determined that the particle counts at the head of the operating table spiked dramatically when laser testing and treatment were accomplished (Table 3). This occurred in spite of air aspiration simultaneous with laser treatment. When the laser stopped firing, the air aspiration also stopped, leaving a visible plume of particulate matter suspended over the head of the operating table. Recovery toward baseline occurred over several

Table 1
Steps Taken or Considered to Solve Diffuse Lamellar Keratitis Mystery

1) Emptying and daily cleaning and drying of sterilizer reservoirs and humidifier reservoirs. Rationale: Prevention of pseudomonas/endotoxin scenario.
2) Use of a preassembled, sterile disposable microkeratome. Rationale: Elimination of technician assembly error and avoidance of contamination.
3) No use of ethylene oxide sterilized instruments or products. Rationale: Residual ethylene oxide on instruments can cause inflammation.
4) Terminal cleaning of LASIK O.R. before each surgery day. Rationale: Elimination of sources of contamination possibly introduced between surgery sessions.
5) Use of disposable cannulas only. Rationale: Avoidance of intraluminal contamination.
6) Use of preservative-free tetracaine in minimal dosage. Rationale: Preserving epithelial integrity reduces DLK.
7) Perilimbal Chayet drains for all cases. Rationale: To prevent introduction of debris onto the corneal bed.
8) Sterile technique with O.R. attire (caps, masks, powder-free gloves, 6-minute scrubs for all O.R. personnel. Patient is gowned and wears a hair net). Rationale: Prevention of infection and minimizing the risk of contamination.
9) Elimination of alcohol foam application to hands between cases. Rationale: The foam emits an odor that might interfere with laser energy transmission and might contaminate the corneal bed.
10) No Betadine in the eye during the pre-surgical prep. Rationale: Betadine can cause inflammation.
11) A trial of lid scrubs and topical antibiotics for 1 week preoperatively for all patients. Rationale: Elimination of lid margin infection as a possible cause of DLK.
12) Isolation of lid margins intraoperatively with Tegaderm drapes to top and bottom lids. Rationale: Prevention of lid margin contamination of the operative site.
13) Instrument cleaning with Universal Instrument Cleaner and distilled water. Use of throwaway toothbrushes to scrub each set of instruments. Rinse instruments sequentially in three trays of distilled water. Dispose of trays after each operating day. Rationale: Tap water may be contaminated. Same for old brushes and trays.
14) Various trials of preoperative anti-inflammatory prophylaxis with topical steroids alone, steroids with non-steroidals, and non-steroidals alone. Rationale: Looking for effective anti-inflammatory activity.
15) Systemic steroid administration (Prednisone 80 mg starting 1 day preoperatively and continuing for 5 days postoperatively). Rationale: Possible reduction or elimination of DLK.
16) Elimination of methylcellulose on the cornea immediately postoperatively. Rationale: Methylcellulose has been reported to cause inflammation if it gets under the flap.
17) Elimination of gentian violet marking of the cornea. Rationale: Gentian violet irritates the corneal epithelium.
18) Steroid solution applied directly to the corneal bed. Rationale: Direct application of steroids might eliminate or minimize DLK. (Don't do this! It incites a severe form of DLK probably from the preservative in the solution.)
19) Elimination of steam sterilization and use of the Cox dry heat sterilizer. Rationale: Total avoidance of the pseudomonas/endotoxin scenario.
20) Substitution of preservative-free acetylcholine instead of pilocarpine to induce preoperative miosis for better laser centration. Rationale: Pilocarpine (with preservative) can cause iritis and therefore might also cause or exacerbate DLK. Acetylcholine is preservative free.
21) Elimination of acetylcholine. Rationale: Even without preservative the acetylcholine might induce an inflammatory response.
22) Total elimination of Betadine and all drops in the entire perioperative period (exception for preservative-free tetracaine required for analgesia) Rationale: Elimination of all irritants and preservatives touching the eye preoperatively, intraoperatively, and postoperatively.
23) Liberal irrigation under flap. Rationale: To wash away any contaminant.
24) Minimal irrigation under the flap. Rationale: Avoidance of back wash of debris from the globe surface entering under the flap while irrigating.
25) Chilled BSS before and after laser application. Rationale: Cooling minimizes inflammation.
26) Fractionation of the delivered laser dose (40 spots, then cool for 5 seconds, then repeat until total dose administered). Rationale: Broad beam lasers may heat the corneal bed when the entire treatment is delivered at once and result in a higher incidence of DLK.
27) Purchase of a flying spot laser. Rationale: Could there be something wrong with the broad beam laser being used that was causing DLK? Of the first 12 eyes treated with the new flying spot laser, 6 developed DLK!
28) Conduct an air quality analysis. Rationale: Could there be some airborne contaminant that deposited itself on the bed of the cornea once the flap was elevated which would then induce DLK? This approach provided unexpected information which led to substantial amelioration of the DLK millstone.

Table 2
Baseline Particulate Levels Before HVAC Repair

Area	Particles/Cubic Centimeter
Third floor main hallway	143,000
LASIK waiting area	96,200
Third floor lecture hall	123,000
LASIK operating room	66,000

Table 3
Treatment-induced Particulate Levels Before HVAC Repair

Event	Particles/ Cubic Centimeter
O.R. particle count before first case	66,000
Particle spike after testing/treatment	322,463
Recovery prior to start of next case	31,575

minutes as the HVAC system drew the contaminated air out of the LASIK operating room. Particle counts also increased when the adjacent equipment room door was opened, implying a higher air pressure in the equipment room than in the operating room itself. According to the consultants, the highest pressure should be in the operating room, so that any contaminants would exit when a door is opened. Adding a return vent in the equipment room would solve this problem.

CO_2 monitoring in the LASIK operating room provided further clues that all was not normal. An average CO_2 level should be in the 700 to 800 ppm range with a maximum of 1000 ppm. The CO_2 level increased throughout the day to a value of 2465 ppm. This finding implied inadequate air exchange in the LASIK suite and explained why personnel complained of fatigue and headaches after a day of LASIK surgery. Expired CO_2 from patients and operating room personnel was accumulating within an apparently closed system. Five fresh air exchanges per hour are desired to keep CO_2 within normal limits. "The solution to pollution is dilution" was the phrase I heard repeatedly that day from the air quality consultant.

After completing surgery, it was time to investigate the HVAC instillation for the LASIK suite. As suspected from measured CO_2 levels, there was no fresh air inlet, nor was there an exhaust to the outside. This was a closed air system that continuously recirculated stale air throughout the LASIK suite. Further, the HEPA air filters were in actuality low quality pleated paper filters of the type supplied with the air conditioning unit. These filters would keep out flies and mosquitoes but not much else! To make matters worse, the HVAC ductwork was layered with sheet rock dust and fiberglass insulation particles, undoubtedly introduced when the facility was built. (The consultant could write his initials with his finger on the inside of the ductwork.) The more the HVAC blower ran, the more sheet rock and fiberglass contamination was circulated throughout the operating room. Without HEPA filtration, this material was not removed from the air but was allowed to deposit itself on the corneal bed when the flap was elevated. This explained the DLK.

Why did the DLK increase over time? Contamination increased because the laser was fired at various testing materials, which created an ever increasing airborne particle load added to the air that was already contaminated with fiberglass and sheet rock particles. There was no HEPA filtration to remove these materials. The more contamination, the more DLK.

Repairs to the LASIK suite HVAC system included instillation of a fresh air inlet and an exhaust outlet, as well as instillation of HEPA filtration. Surprisingly, after instillation it was discovered that the HEPA filters were incorrectly installed downstream of the operating room, allowing unfiltered outside air to enter the operating room. This was immediately rectified by moving the HEPA filter upstream of the operating room. Pressure balancing throughout the LASIK suite was accomplished so that the greatest air pressure was in the operating room itself. All ductwork was tested for airtight joints. Gaskets were installed in the filter access doors to prevent any contamination from the bowels of the building finding its way into the system. A heating coil was installed within the supply ductwork to preheat the cold outside air delivered to the operating room. The ductwork was professionally cleaned with sterilized wands and HEPA filtered vacuum cleaners. The operating room personnel were instructed to run the HVAC system in continuous mode during surgery days, to constantly draw in fresh filtered air.

Following these repairs, air quality was rechecked during subsequent LASIK surgery (Table 4). Baseline particulate levels were now reduced by 99%. The treatment-induced particulate spike rose to 73.5% of before repair levels, but within several minutes, recovery brought the level down to 3% of that experienced before the repairs were made.

In reviewing the situation, it is fortunate that flap lifting and irrigation, when required to treat DLK, was performed in the downstairs ambulatory surgery unit because of better optics with that operating microscope. The ASU air handling system was installed correctly and lifting the flap in that clean environment did not reinoculate the corneal bed with contaminants. A return to the LASIK suite for flap lifting would presumably not have been as successful.

Intuitively, it seems that sheet rock dust, fiberglass particles, and lasered testing substrate, if deposited on the corneal bed, could incite an

Table 4
Treatment-induced Particulate Levels After HVAC Repair

Event	Particles/ Cubic Centimeter
O.R. particle count before first case	535
Particle spike after testing/treatment	237,117
Recovery prior to start of next case	987

inflammatory reaction. It seems reasonable to suggest that all new LASIK facilities have a baseline investigation of the integrity and cleanliness of the environmental control system by air quality monitoring prior to undertaking surgery. Air quality monitoring would also seem to be worthwhile as part of any investigation of high DLK rates. Routine periodic cleaning of HVAC ductwork seems only prudent in light of our experience. Local hospitals can provide sources of expertise for HVAC instillation, maintenance, and air quality monitoring. Laser manufacturers should consider increasing the vacuum on their air aspirating systems, as well as installing a time delay to allow the system to continue cleaning the air for a period of time after the laser stops firing, in order to reduce the observed particulate level spike associated with firing the laser.

The ultimate question is, did the DLK rates decrease with the improvement in air quality? The answer initially was a resounding yes, with total elimination of DLK for a short period of time, but subsequently rates have risen to a value of about half of what was previously experienced. Cleaning the air helped, but something else remains! The mystery continues, and I have run out of ideas except to play my trump card. I now perform LASEK exclusively, and have solved the DLK issue by this end run approach.

Editor's Note:

Publishing an anonymous article in which the author is not identified in a peer reviewed journal may seem inconsistent. However, this mysterious tale can, I believe, be extremely instructive for all readers, especially since it leads to no firm, clear-cut conclusion. I expect considerable correspondence after this article is published. The author requested anonymity for one simple reason: the risk of exposure for litigation with such an honest and revealing narrative. After consultation with members of the JRS Editorial Board, I decided to publish the anonymous article for the potential benefit of readers of JRS, who I am sure will understand the circumstances.

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