

Surgical Glove–Associated Diffuse Lamellar Keratitis

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Purpose: To demonstrate a potential cause of a prolonged epidemic of diffuse lamellar keratitis (DLK).

Method: This retrospective review analyzed an epidemic of diffuse lamellar keratitis over a 3-year period in a single surgery center. Altering the brand of surgical gloves used during surgery was associated with an elimination of the DLK epidemic. Optical microscopy, scanning electron microscopy–energy dispersive spectroscopy (SEM-EDS), and Fourier transform infrared (FTIR) spectroscopy were performed on both brands of surgical gloves to allow for comparisons and determine possible surface contaminants responsible for the DLK outbreaks.

Results: The incidence of DLK during the epidemic ranged from 2% to 38% on a quarterly basis for the 3-year period. A change in the brand of surgical gloves resulted in a cessation of DLK. Surface analysis of both brands of gloves revealed extensive silicone oil contamination on the internal and external surfaces of the DLK-associated gloves and insignificant amounts of silicone oil on the external surface of the DLK-free gloves.

Conclusion: Silicone oil contamination of surgical gloves appears to be associated with epidemic DLK.

Key Words: diffuse lamellar keratitis, Sands of the Sahara, silicone oil, surgical glove, LASIK complications

(*Cornea* 2005;24:699–704)

Diffuse lamellar keratitis (DLK) is a noninfectious condition that develops within the keratectomy interface after laser-assisted in-situ keratomileusis (LASIK).¹ Our current understanding of DLK is that it occurs secondary to an inciting agent or event, perhaps enhanced in an individual with a

predisposed immune system.^{2–4} The possible inciting agents for DLK include interface debris in the form of meibomian secretions, blood, microkeratome oil, silicates, wax, povidone iodine, carboxymethylcellulose, cleaning solutions, and bacterial endotoxins.^{5–12} Although the condition can develop many months after LASIK when subsequent trauma, epithelial abrasions, or iritis develops,^{13–23} it has classically been described as a condition appearing several days following the LASIK procedure. DLK can occur as sporadic cases or in epidemic clusters.²⁴

Between the years 2000 and 2003, our practice experienced an increased incidence of epidemic DLK that was unresponsive to changes in instrumentation or technique. During this time period, attempts to eliminate epidemics included switching from detergent instrument cleaners to enzymatic cleaners, discontinuation of betadine preps, changing sterilizers, and switching microkeratomes. No appreciable or dramatic change in the incidence of DLK resulted from these modifications.

In September 2003, we became aware of the possible association of surgical glove contamination as an etiology for DLK (D. Hatsis, "Sands of the Sahara Syndrome: A Refractive Emergency." Presented at the ASOA Clinical & Surgical Program, Philadelphia, June 2, 2002). We report herein the effects of changing the brand of surgical gloves used to perform LASIK in regard to the incidence of epidemic DLK. A thorough analysis and discussion of possible surface contaminants for each brand of glove and their potential association with DLK is also presented.

PATIENTS AND METHODS

A review of our LASIK and LASIK enhancement cases between January 2000 and March 2004 was performed. Our routine operative preparation on the day of surgery included a prep with povidone iodine (Betadine[®]) and draping of the eyelids with Tagaderm[®] to isolate the lids and lashes from the operative field. Following topical anesthesia with 1 drop of proparacaine 0.5%, a nonaspirating lid speculum was placed. Marking of the corneal surface with gentian violet on a Hoffman-Buratto marker (ASICO AE-2817) was followed by placement of a Hansatome[®] (Bausch & Lomb) microkeratome, balanced salt solution (BSS) for topical lubrication, and creation of the keratectomy. A moist technique was used by wringing out a BSS-soaked Merocel[®] sponge with gloved fingers and wiping the interface bed once with the moistened sponge immediately before laser application. Laser treatment was performed with either the VISX[™] S3 or S4 excimer laser.

Received for publication July 14, 2004; revision received October 1, 2004; accepted October 21, 2004.

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Expenses for independent laboratory analysis of the surgical gloves were compensated for retroactively by an educational grant from Cardinal Health, Inc.

None of the authors has any financial interest in any of the products mentioned in this manuscript.

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Following treatment, all flap interfaces were irrigated with either BSS or lactated Ringer solution. After the flap was repositioned, patients were given several drops of ofloxacin (Ocuflox[®]), prednisolone phosphate 1%, and diclofenac sodium 0.1% (Voltaren[®]) intraoperatively. Postoperatively, the patients were immediately begun on a regimen of prednisolone acetate 1% (Pred Forte[®] 1%) 4 times a day, Ocuflox[®] 4 times a day, Voltaren[®] 4 times a day as needed for discomfort, and frequent nonpreserved artificial tears. Any patients with concomitant corneal abrasions were treated with a Plano-T bandage contact lens (Bausch & Lomb) if more than 20% of the corneal epithelium was abraded.

Between January 2000 and September 2003, various temporary alterations in the routine preoperative and intraoperative preparations were made. These alterations were made one at a time to better isolate the offending agent responsible for the DLK epidemics.

These alterations included the following. Five-minute steam sterilization times were increased to 10 minutes. Steam sterilization with an Amsco Eagle Series 2011 (Steris Corporation, Mentor, OH) was temporarily replaced with a portable Statum 2000 sterilizer (SciCan, Pittsburgh, PA) with a fresh reservoir tank. Microkeratome cleaning with Palmolive detergent cleaner was changed to enzymatic cleaner, and additional rinsing cycles were instituted. Preoperative povidone iodide and intraoperative antibiotics, steroids, and nonsteroidals were temporarily discontinued and then resumed. The Hansatome microkeratome (Bausch & Lomb) was replaced with an Amadeus microkeratome (Advanced Medical Optics, Santa Ana, CA) and then later resumed utilizing zero-compression heads. None of these alterations appeared to have any significant effect on the incidence of DLK.

Encore Microptic surgical gloves (Ansell Healthcare Products Inc, Red Bank, NJ) were used for all procedures before September 2003. Lot 03 01002705 Encore Microptic gloves were used between January 2003 and September 2003. The lot numbers for Encore Microptic gloves before January 2003 were indeterminate. In September 2003, surgical gloves were switched to Protegrity SMT (Lot 09 TS0305339) (Cardinal Health Inc, Dublin, OH). An analysis of the incidence of DLK for patients undergoing LASIK between January 2003 and March 2004 (when there was certainty regarding glove lot numbers) was performed.

Surface Analysis

A thorough analysis of fingertip samples of each glove brand was performed by an independent laboratory (MEI-Charlton, Inc, Portland, OR). The unopened sterile packaged gloves were shipped to the laboratory with instructions to analyze the surfaces of both brands and determine differences. The laboratory was blinded to which glove brand might be associated with the DLK epidemics.

Glove samples were analyzed by optical microscopy, scanning electron microscopy dispersive spectroscopy (SEM-EDS), and Fourier transform infrared (FTIR) spectroscopy. The FTIR surface analysis was conducted by comparing transmission spectra with attenuated total reflection spectra.

RESULTS

The incidence of DLK between January 2000 and September 2003 ranged between 2% and 38% when examined on a quarterly basis (Fig. 1). Fifteen of the 99 cases of DLK (15%) were associated with corneal abrasions. No corneal abrasions developed following the second quarter of 2001, coinciding with the introduction of low-compression heads on the Hansatome microkeratome. DLK persisted until the fourth quarter of 2003 despite the elimination of corneal abrasions.

Surgical days beginning in January 2003 were evaluated independently because certainty regarding the lot number for the Encore Microptic gloves was assured. The incidence of DLK during this time period ranged from 0 to 83% on a daily basis, with the surgical day immediately preceding alteration in glove brands demonstrating 5 cases of DLK out of 6 eyes undergoing surgery (Fig. 2). Following discontinuation of the Encore Microptic gloves and institution of Protegrity gloves, DLK was eliminated except for 1 case of faint stage 1 DLK. This 1 case of DLK completely resolved by the third postoperative day with use of topical prednisolone acetate 1% every hour while awake. There was no change in technique during or following this period when glove brands were changed. The incidence of DLK in eyes utilizing Encore Microptic gloves was 37% (28/76), and the incidence in the Protegrity eyes was 0.9% (1/116). The difference between the 2 groups of eyes was statistically significant ($P < 0.001$).

Surface analysis of each brand of surgical glove was performed by an independent laboratory. Optical microscopy of the Protegrity glove revealed a very fine powdery material on the exterior surface. This was confirmed with SEM photographs (Fig. 3). FTIR spectroscopy showed the surface material to be a carbonate, and the SEM-EDS analysis showed that the surface material was a calcium salt (Fig. 4). The FTIR spectrum of the bulk glove material showed a peak at 2236 cm^{-1} , which was reported likely to be a small amount of isocyanate compound used as a rubber additive. No isocyanates were found on the surface. Although there was some signal present in the

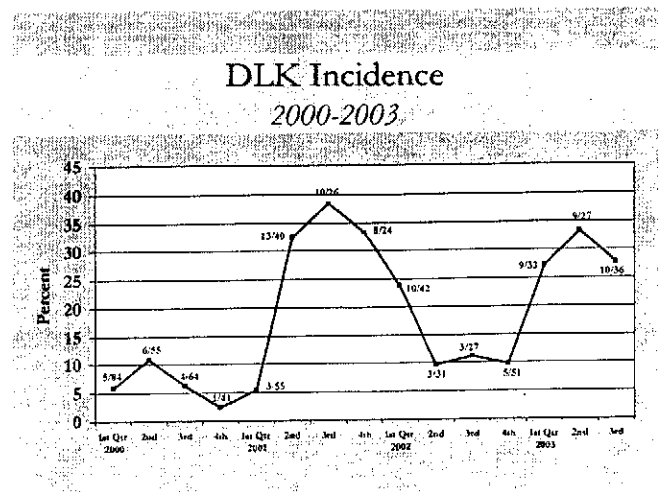


FIGURE 1. Quarterly incidence of DLK from 2000–2003. Each data point represents number of DLK cases per total number of eyes treated in that quarter.

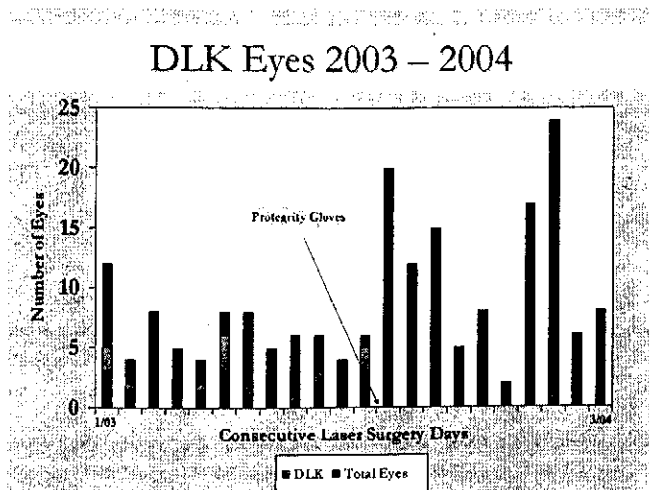


FIGURE 2. Number of DLK eyes (gray) as a fraction of total eyes (black) undergoing LASIK on individual consecutive surgery days from January 2003 to March 2004. Discontinuation of Encore Microptic gloves for Protegrity gloves demonstrates an almost total cessation of DLK.

silicone range on the SEM-EDS, the surface FTIR spectra indicated “some” silicone oil on the internal surface of the glove but insignificant levels on the exterior surface.

Optical microscopy of the Encore Microptic gloves showed a textured but otherwise smooth exterior surface. SEM photographs confirmed no gross abnormalities of the surface (Fig. 5). FTIR spectroscopy showed silicone oil as a major surface component. The internal surfaces had more silicone oil than the exterior surface. SEM-EDS analysis showed aluminum, calcium, and sulfur in the bulk rubber whereas silicon and chlorine were enriched on the surface (Fig. 6).

A laboratory summary of the differences between the external surfaces of both brands demonstrated calcium carbonate powder on the surface of the Protegrity gloves not present on

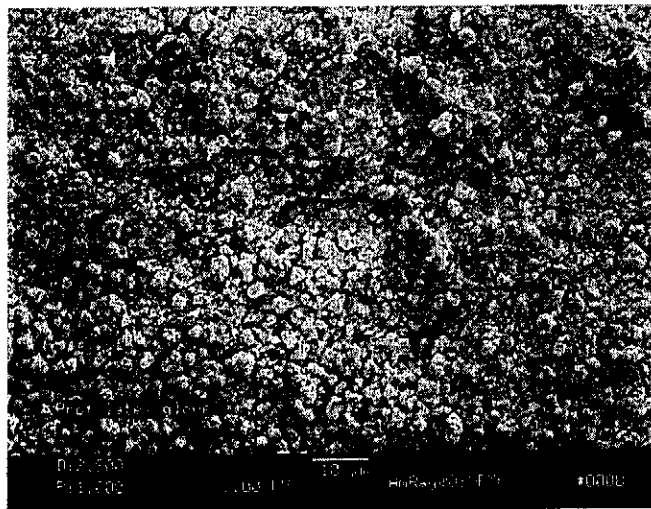


FIGURE 3. Scanning electron micrograph of exterior surface of Protegrity glove ($\times 1000$). Note powdery granules.

the Encore Microptic gloves. Silicone oil was reported as a major surface contaminant on the Encore Microptic gloves but to be present only in insignificant quantities on the Protegrity gloves.

DISCUSSION

Epidemics of DLK are a source of frustration for both the operating surgeon and operating room staff. Although the potential for significant morbidity exists for the patient, if diagnosed early and treated appropriately, excellent results are the usual outcome.²⁵ Sporadic episodes of DLK can occur from numerous etiologies. However, when epidemics develop, there is an implication that a single source is responsible for the outbreak, and pinpointing that source can be challenging.

A systematic approach of eliminating or changing a potential source for DLK was undertaken beginning in 2000. These changes were made one at a time every few months while the other variables remained unchanged as controls. In this manner, a sudden diminution in the incidence of DLK coinciding with a change in technique or instrumentation would implicate that variable as a potential source of DLK. An accurate timeline of exactly when these variations were made was not recorded other than the approximate date of institution of zero-compression heads on the Hansatome microkeratome (third quarter of 2001). Despite the concurrent cessation of corneal abrasions (a known risk factor for DLK) in the third quarter of 2001, the incidence of DLK was not acutely affected at this time, suggesting that the eventual eradication of DLK in 2003 was not related to the earlier elimination of abrasions.

One of the most popular etiologies to be recently implicated as a cause of epidemic DLK has been bacterial endotoxins. An attempt to eliminate endotoxins as a possible source of DLK within this practice by increasing sterilization times and changing sterilizers had no apparent effect on the incidence of DLK. Similarly, eliminating povidine iodide, intraoperative medications, and alternating microkeratomes had no demonstrable effect either.

Initially, when the concept that the surgical gloves might be a source of DLK was suggested, skepticism was the initial response. After all, the surgical gloves were sterile and talc-free and did not directly come into contact with the keratectomy interface or the ocular surface. On further inspection, however, it became apparent that the gloves were in contact with the surgical instruments and sponges that were then coming into direct contact with the interface (Fig. 7). Perhaps the greatest potential source of contamination may have occurred when the wet Merocel[®] sponge was compressed to create a slightly moistened consistency and then wiped directly onto the stromal bed before laser application. Silicone oil could easily be transferred from the gloves to the interface and remain in significant quantities, despite irrigation, to elicit an inflammatory response.

The profound change in incidence of DLK following cessation of Encore Microptic gloves and institution of Protegrity SMT gloves strongly suggests a contaminant on the Encore Microptic gloves as the source for DLK. Statistical analysis for only those eyes undergoing surgery in 2003–2004 seemed appropriate because certainty regarding glove lot numbers and their relationship with subsequent glove analysis

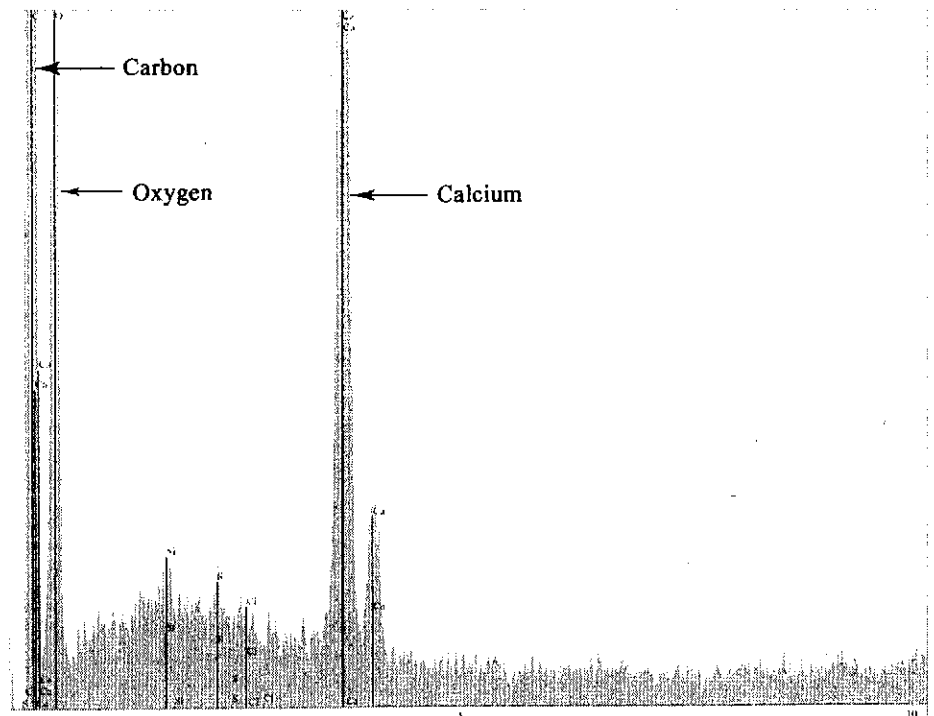


FIGURE 4. SEM/x-ray energy spectrometry of Protegrity glove. Major peaks at carbon, oxygen, and calcium.

was insured. Analysis of the surface of both gloves was performed with the thought that any differences between the 2 gloves would isolate the offending agent. A substance found on the Encore Microptic gloves not present on the Protegrity gloves would strongly implicate this substance as a potential etiology for DLK. Conversely, any substance found on the Protegrity gloves that was not present on the Encore Microptic gloves would not be a potential agent for DLK but could remotely represent a protective agent for the prevention of DLK.

The only significant difference between the 2 glove brands was the presence of large quantities of silicone oil on

the exterior surface of the Encore Microptic gloves and calcium carbonate powder on the exterior surface of the Protegrity gloves. Calcium carbonate (chalk) is commonly used in glove manufacturing as a substance placed on the glove former or mold that allows for easy removal of the glove once curing is completed. Although gloves may be labeled as “powderless” or “powder-free,” this is usually in reference to significant quantities of cornstarch or talcum powder (hydrous magnesium silicate), the latter of which has been associated with inflammatory granulomas and adhesion formation. According to American Society for Testing and Materials (ASTM) standards, dusting or mold-release compounds may still exist in small quantities on powder-free gloves.²⁶ Although talc has been implicated as a possible etiology for DLK,²⁷ calcium carbonate has not, and its presence on the DLK-free Protegrity gloves suggests that calcium carbonate is not an associated risk factor for the development of DLK.

Silicone oil may be used in 2 different steps of the glove-manufacturing process. Silicone may be added to the coagulant or the latex as a defoamer. These formulations tend to be proprietary, and little is known about them. Despite this, they are very effective so that only small quantities are generally needed. Thus, their final concentration in gloves is typically very low, and this source of silicone is unlikely to be the cause for large quantities of silicone on the glove surface.

Silicone oil is also used as part of a polymer-based donning coating that allows the surgeon's hands to enter and exit from the gloves without the use of powders. It also acts to prevent gloves from sticking during the manufacturing process. The materials in these coatings are either mostly or completely methyl silicones. If the surgical glove is reverse-stripped (turned inside-out) off of the former or mold, the donning coating is added as a final dip before the final drying/curing

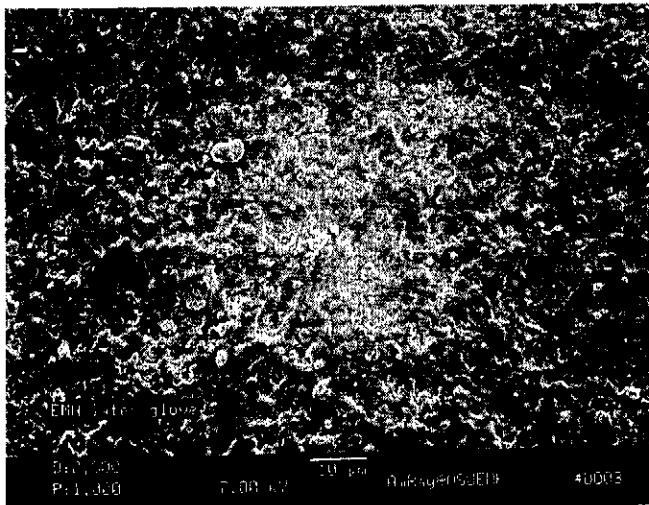


FIGURE 5. Scanning electron micrograph of exterior surface of Encore Microptics glove ($\times 1000$).

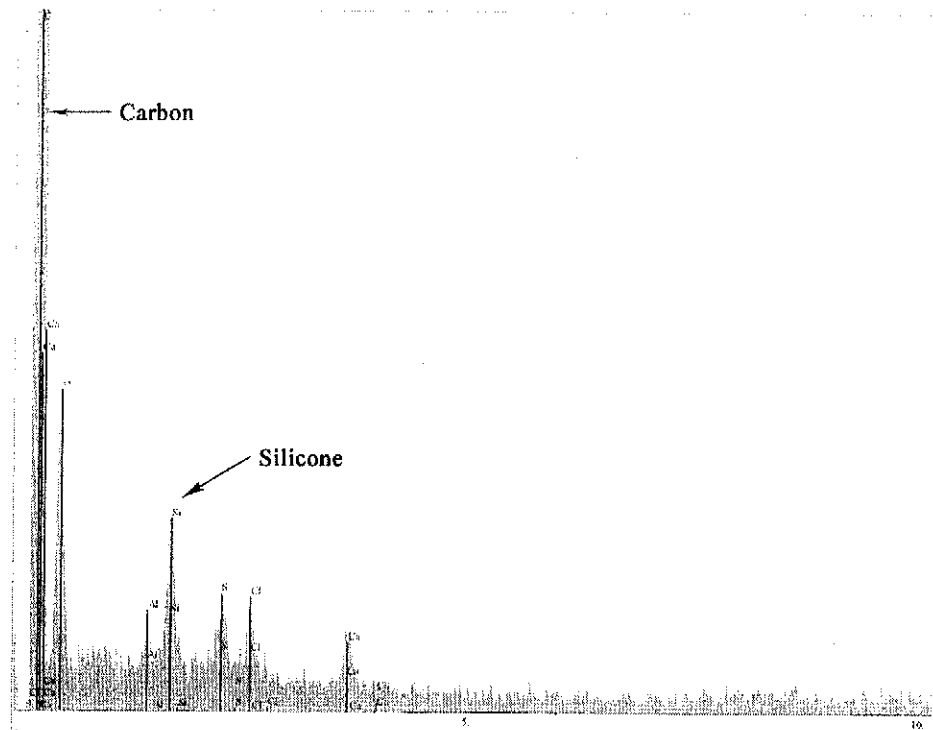


FIGURE 6. SEM/x-ray energy spectrometry of Encore Microptic glove. Note peak in silicon.

of the coagulated latex. This should allow the inside of the glove to have a lubricating coating with no donning coating on the outside of the gloves.²⁶

The implication that silicone oil on the exterior surface of the Encore Microptic gloves was responsible for the epidemics of DLK stems from the lack of silicone oil on the exterior of the Protegrity gloves and the almost complete

cessation of DLK after exchanging Encore Microptic for Protegrity gloves. Oils have been implicated in other studies as a potential inciting agent for DLK. One of the first descriptions of the “Sands of the Sahara Syndrome” was given by Robert Maddox, MD, and was eventually believed to result from silicone oils leaking from the motor of a Hansatome microkeratome (R. Maddix, personal communication, May 2, 2004;

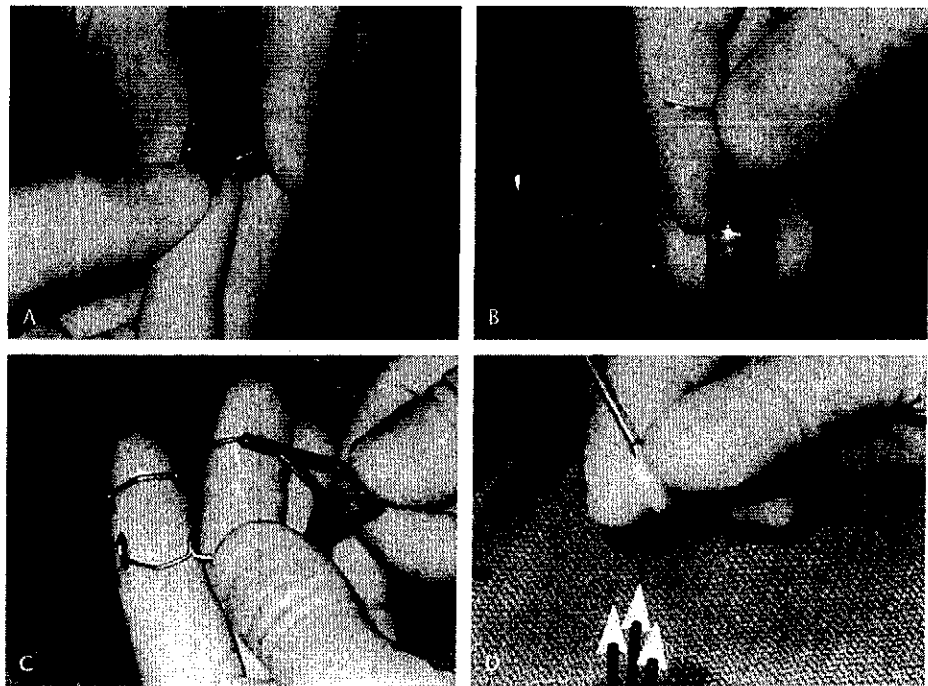


FIGURE 7. Potential sources of instrument contamination with surgical gloves including microkeratome blade (A), irrigating cannula (B), eyelid speculum (C), and Merocel sponges (D).

R. Maddox and A. Hatis, "Sands of the Sahara," poster presented at the ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Diego, April 1998). Oils present on microkeratome blades have also been implicated as a source for DLK.^{28,29}

Assuming that silicone oil contamination is the major etiology for DLK in this study, it is possible that the variations in the incidence of DLK between 2000 and 2003 (Fig. 1) may be explained by varying degrees of silicone oil contamination on different glove lot numbers or different glove pairs within the same lot numbers used during this extended period. Certainty regarding the contaminated glove lot number and the subsequent surface analysis demonstrating significant oil concentrations was known only for the period beginning in January 2003. Thus, DLK that presented before 2003 can only be assumed to be secondary to similar but variable levels of silicone oil contamination in other Encore Microptic glove shipments.

The obvious limitation of this study is the need for sequential elimination of potential causes of DLK followed by an evaluation of the effect of changing these variables. An ideal study would be prospective and compare 2 groups of patients undergoing LASIK utilizing either of the 2 glove brands in a double-blind study. Unfortunately, because of the strong correlation of the Encore Microptic gloves with the DLK epidemic, a controlled study would be unethical, especially considering the rare but potential risk of significant ocular morbidity from the development of severe DLK. The thought of challenging a small group of patients with the DLK-associated gloves on a single surgery day was also considered but abandoned for the same ethical reasons.

At present, we believe that the presence of silicone oil on the surface of surgical gloves is a significant risk factor for the development of DLK. Definitive animal studies to further substantiate these findings are planned for the future.

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