

Heading Off Acute Postop Endophthalmitis

Incision site and proper wound construction are key tools in the prevention of acute postoperative endophthalmitis.

THE TEMPORAL CLEAR CORNEAL incision for cataract removal and intraocular lens implantation is slowly but surely becoming the surgical technique of choice for many ophthalmologists.

Fifty-seven percent of physicians in the 2002 survey of the American Society of Cataract and Refractive Surgery say they perform clear corneal incisions—up from 47 percent in 2000. The surgical technique was preferred by 66 percent of surgeons performing more than 25 cataract procedures per month—up from 56 percent in 2000. Use of a temporal incision increased with cataract surgery volume.

Along with the gradual acceptance of temporal clear corneal incisions, however, recent studies report that they are associated with a higher risk of acute postoperative endophthalmitis.^{1,2}

"Endophthalmitis is the most dreaded complication following cataract surgery," says Robert H. Osher, MD, professor of ophthalmology at the University of Cincinnati and medical director emeritus at the Cincinnati Eye Institute. "The only thing worse would be me dying in the operating room! Aside from this adverse event, endophthalmitis is right up there."

In this article, surgeons share their reactions to the reports of higher endophthalmitis risk associated with temporal

clear corneal incisions and whether the findings affect their preference for performing the procedure. They also review the important steps to take in lowering its incidence: choosing the safest incision site and paying careful attention to wound construction.

The Case for Clear Cornea

Studies report that endophthalmitis incidence following cataract surgery is relatively uncommon—between 0.08 percent and 0.30 percent. Trouble is,

the research shows a disproportionately higher risk of the complication after temporal clear corneal procedures. Researchers at the Barnes Retina Institute

in St. Louis saw a three-fold increased incidence of endophthalmitis following clear corneal incisions when compared to scleral tunnel wounds in a retrospective, case-control study.³

Still, many physicians remain loyal to the surgical technique.

Proponents say clear corneal wounds heal quickly. They don't bleed, so the eye remains white after surgery. The technique is more comfortable postoperatively for patients and requires less

Judith Springer Riddle
Associate Editor

James P. Gills, MD



Acute postoperative endophthalmitis incidence following cataract surgery is relatively uncommon—between 0.08 percent and 0.30 percent.

operating-room time than scleral tunnel procedures. Physicians also say they have better anterior-chamber access, astigmatism control, the choice of topical anesthesia instead of retrobulbar or peribulbar blocks, and they don't have to cauterize, use scissors or forceps during the surgery.

"The theory that clear corneal incisions are more likely to lead to endophthalmitis is a big area of debate," says William Trattler, MD, an ophthalmologist at the Center for Excellence in Eye Care in Miami. "I don't believe that one incision type is better than another in avoiding endophthalmitis. Depending on who's doing the surgery, the rate of endophthalmitis can be



The clear corneal surgical technique is gaining in popularity among ophthalmologists. But studies show that clear corneal incisions are a risk factor for endophthalmitis.

20 times higher than that of another doctor [or center]. One big factor is wound construction. The clear corneal incisions that result in endophthalmitis are poorly constructed. If one study shows a higher rate, then we need to know how the incisions were created. It's possible to construct a very stable clear corneal wound. Attention to detail is important."

John F. Sciarrino, MD, an ophthalmologist at Northridge Eye Center in Ft. Lauderdale, Fla., says that because of the low endophthalmitis risk following clear corneal incisions, as indicated in the studies, widespread use of the technique is warranted. Dr. Sciarrino believes the studies don't really establish that clear corneal wounds are more prone to infection than scleral tunnel procedures, and that the evidence is conflicting and inconclusive. "Clear cornea is the predominant technique used by surgeons for cataract surgery," says Dr. Sciarrino. "I think if there were really a higher incidence of endophthalmitis, we wouldn't do it. This is a topic that's very controversial."

Investigators from the Barnes Retina Institute study concluded that results from retrospective case-control studies indicating an increased risk of endophthalmitis after clear corneal surgeries must be interpreted cautiously, and that their findings aren't necessarily an indictment of the technique.

Brimonidine Tartrate Ophthalmic Solution 0.2%

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Each mL Contains:

ACTIVE: Brimonidine tartrate: 0.2% (2 mg/mL).

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PRESERVATIVE ADDED: Benzalkonium Chloride (0.05 mg).

CLINICAL PHARMACOLOGY:

Mechanism of Action:

Brimonidine tartrate ophthalmic solution 0.2% is an alpha adrenergic receptor agonist. It has a peak ocular hypotensive effect occurring at two hours post-dosing. Fluorophotometric studies in animals and humans suggest that brimonidine tartrate has a dual mechanism of action by reducing aqueous humor production and increasing uveoscleral outflow.

Clinical Evaluations:

Elevated IOP presents a major risk factor in glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss. Brimonidine tartrate has the action of lowering intraocular pressure with minimal effect on cardiovascular and pulmonary parameters.

In comparative clinical studies with timolol 0.5%, lasting up to one year, the IOP lowering effect of brimonidine tartrate ophthalmic solution 0.2% was approximately 4-6 mmHg compared with approximately 6 mmHg for timolol. In these studies, both patient groups were dosed BID; however, due to the duration of action of brimonidine tartrate ophthalmic solution 0.2%, it is recommended that brimonidine tartrate ophthalmic solution 0.2% be dosed TID. Eight percent of subjects were discontinued from studies due to inadequately controlled intraocular pressure, which in 30% of these patients occurred during the first month of therapy. Approximately 20% were discontinued due to adverse experiences.

INDICATIONS AND USAGE:

Brimonidine tartrate ophthalmic solution 0.2% is indicated for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The IOP lowering efficacy of brimonidine tartrate ophthalmic solution 0.2% diminishes over time in some patients. This loss of effect appears with a variable time of onset in each patient and should be closely monitored.

CONTRAINDICATIONS:

Brimonidine tartrate ophthalmic solution 0.2% is contraindicated in patients with hypersensitivity to brimonidine tartrate or any component of this medication. It is also contraindicated in patients receiving monoamine oxidase (MAO) inhibitor therapy.

PRECAUTIONS:

General:

Although brimonidine tartrate ophthalmic solution 0.2% had minimal effect on blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.

Brimonidine tartrate ophthalmic solution 0.2% has not been studied in patients with hepatic or renal impairment; caution should be used in treating such patients.

Brimonidine tartrate ophthalmic solution 0.2% should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension or thromboangiitis obliterans.

During the studies there was a loss of effect in some patients. The IOP-lowering efficacy observed with brimonidine tartrate ophthalmic solution 0.2% during the first month of therapy may not always reflect the long-term level of IOP reduction. Patients prescribed IOP-lowering medication should be routinely monitored for IOP.

Information for Patients:

The preservative in brimonidine tartrate ophthalmic solution 0.2%, benzalkonium chloride, may be absorbed by soft contact lenses. Patients wearing soft contact lenses should be instructed to wait at least 15 minutes after instilling brimonidine tartrate ophthalmic solution 0.2% to insert soft contact lenses.

As with other drugs in this class, brimonidine tartrate ophthalmic solution 0.2% may cause fatigue and/or drowsiness in some patients. Patients who engage in hazardous activities should be cautioned of the potential for a decrease in mental alertness.

Drug Interactions:

Although specific drug interaction studies have not been conducted with brimonidine tartrate ophthalmic solution 0.2%, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered. Alpha-agonists, as a class, may reduce pulse and blood pressure. Caution in using concomitant drugs such as beta-blockers (ophthalmic and systemic), antihypertensives and/or cardiac glycosides is advised. Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with brimonidine tartrate ophthalmic solution 0.2% in humans can lead to resulting interference with the IOP lowering effect. No data on the level of circulating catecholamines after brimonidine tartrate ophthalmic solution 0.2% are available. Caution, however, is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

ADVERSE REACTIONS:

Adverse events occurring in approximately 10-30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus.

Events occurring in approximately 3-9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.

The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness and syncope.

The following events have been identified during post-marketing use of brimonidine tartrate ophthalmic solution 0.2% in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to brimonidine tartrate ophthalmic solution 0.2%, or a combination of these factors, include: bradycardia; hypotension; iritis; miosis; skin reactions (including erythema, eyelid pruritis, rash, and vasodilation); and tachycardia. Apnea, bradycardia, hypotension, hypothermia, hypotonia, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solution 0.2%.

OVERDOSAGE:

No information is available on overdosage in humans. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

DOSAGE AND ADMINISTRATION:

The recommended dose is one drop of brimonidine tartrate ophthalmic solution 0.2% in the affected eye(s) three times daily, approximately 8 hours apart.

Brimonidine tartrate ophthalmic solution 0.2% may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic product is being used, the products should be administered at least 5 minutes apart.

Storage: Store between 15° - 25°C (59° - 77°F).

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So there's still a strong case to be made for clear cornea, says Mark Packer, MD, clinical assistant professor of ophthalmology at Oregon Health & Science University, and an ophthalmologist in private practice in Eugene, Ore. "We don't absolutely know whether there is a higher incidence of endophthalmitis," says Dr. Packer. "There are 2.5 million cataract surgeries done in the United States every year, half of which are clear corneal incisions, so that might be why it appears as though there is a higher incidence."

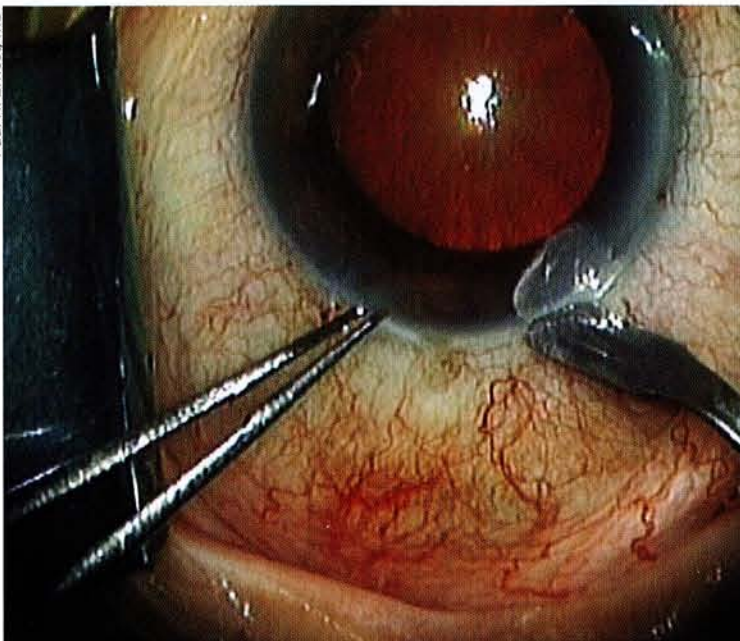
Incision Site

Some surgeons who don't embrace temporal clear corneal procedures say they're comfortable with using their current surgical technique—a scleral tunnel incision for instance—and refuse to switch. Others have abandoned the clear cornea in favor of limbus-based wounds and slight variations of the scleral tunnel maneuver that studies have shown are stronger, more stable and offer greater protection against postop endophthalmitis infection.

Paul H. Ernest, MD, a cataract surgeon and founder of TLC Eyecare & Laser Centers, in Jackson, Mich., has conducted numerous studies on wound construction and strength. Dr. Ernest's work has shown that anterior-limbal incisions offer greater stability than clear corneal wounds and are just as efficient and aesthetically designed.⁴

Anterior-limbus incisions also have been shown to heal faster than clear corneal wounds. An earlier multicenter

Paul H. Ernest, MD



Research shows that anterior-limbal-corneal incisions offer greater stability than clear corneal wounds and are just as efficient and aesthetically designed.

trial, led by Dr. Ernest, compared the healing processes of avascular and vascular incisions. He reported that limbal wounds histologically sealed in a maximum of seven days compared to clear corneal incisions that took as long as 30 to 60 days to heal, leaving more room for endophthalmitis infection.⁵

Studies also show that sclerocorneal-based procedures are associated with a lower endophthalmitis incidence. Results from a recent Japanese clinical trial reported that superior sclerocorneal wounds were 4.6 times less likely to result in a postop endophthalmitis infection than temporal clear corneal incisions.¹ A German study that evaluated the risk factors for endophthalmitis also found that there was a lower risk following sclerocorneal surgeries.²

James P. Gills, MD, clinical professor of ophthalmology at the University of South Florida, and founder/director of St. Luke's Cataract and Laser Institute in Tarpon Springs, Fla., performs what he calls scleral-limbal-corneal (SLIC), or near clear corneal incisions, to ensure a stable and well-sealed wound.

Dr. Gills says creating a watertight incision prevents most bacteria from entering the eye, which isn't always achieved in clear corneal surgeries. Entering through the sclera creates a conjunctival flap that speeds healing and protects against endophthalmitis. "The studies reporting a higher incidence of endophthalmitis following clear corneal incisions are truthful, he says. "The procedure is not always safe in everyone's hands. It requires a different set of surgical skills." The

SLIC incision gives physicians all the benefits of a clear corneal wound, but offers more protection, says Dr. Gills.

Michael McFarland, MD, an ophthalmologist in private practice in Pine Bluff, Ark., is a strong supporter of scleral-limbal-based incisions in light of the possible increased endophthalmitis risk associated with clear corneal procedures. He says the safest place to make an incision is in the limbus. "It's watertight without hydration," says Dr. McFarland. "It doesn't induce astigmatism, and the conjunctiva provides a natural barrier to infection. There's no reason to go through the cornea. The sclera is so much more forgiving. It has a blood supply so it heals quickly. The cornea doesn't, so it takes longer to heal."

Eric Donnenfeld, MD, co-chairman of cornea and external disease at Manhattan Eye, Ear and Throat Hospital in New York City, advocates using a superior clear corneal incision over the temporal location to lower endophthalmitis risk. "There may be less chance for an infection with a superior incision because the wound isn't bathed by the tear



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DESCRIPTION

PATANOL® (olopatadine hydrochloride ophthalmic solution) 0.1% is a sterile ophthalmic solution containing olopatadine, a relatively selective H₁-receptor antagonist and inhibitor of histamine release from the mast cell for topical administration to the eyes.

INDICATIONS AND USAGE

PATANOL (olopatadine hydrochloride ophthalmic solution) 0.1% is indicated for the treatment of the signs and symptoms of allergic conjunctivitis.

CONTRAINDICATIONS

PATANOL is contraindicated in persons with a known hypersensitivity to olopatadine hydrochloride or any components of PATANOL.

WARNINGS

PATANOL is for topical use only and not for injection or oral use.

PRECAUTIONS

Information for Patients: To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

Patients should be advised not to wear a contact lens if their eye is red. PATANOL® should not be used to treat contact lens related irritation. The preservative in PATANOL, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red should be instructed to wait at least ten minutes after instilling PATANOL before they insert their contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size, these doses were 78,125 and 31,250 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of 62,500 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of 7,800 times the maximum recommended ocular human use level.

Pregnancy: Pregnancy Category C. Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 93,750 times the MROHD and rabbits treated at 400 mg/kg/day, or 62,500 times the MROHD, during organogenesis showed a decrease in live fetuses. There are, however, no adequate and well controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Nursing Mothers: Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PATANOL is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

ADVERSE REACTIONS

Headaches have been reported at an incidence of 7%. The following adverse experiences have been reported in less than 5% of patients: Asthenia, blurred vision, burning or stinging, cold syndrome, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, nausea, pharyngitis, pruritus, rhinitis, sinusitis, and taste perversion. Some of these events were similar to the underlying disease being studied.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye two times per day at an interval of 6 to 8 hours.

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Revised: April 2000

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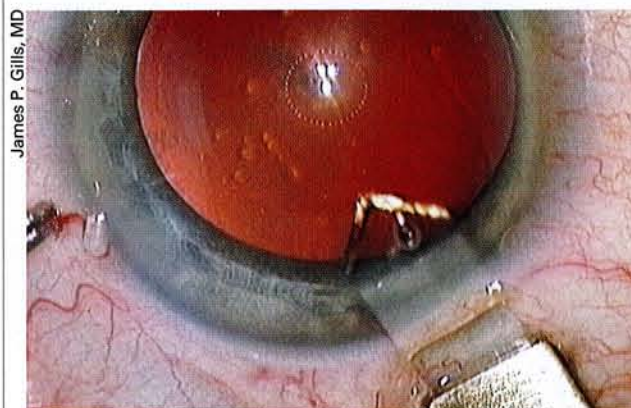
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3. Scott-Levin's *Source Prescription Audit* (SPA) from Verispan, L.L.C., March 1997-October 2002.

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REVIEW COVER STORY



James P. Gills, MD

Scleral-limbal-corneal incisions (SLIC) ensure a stable and well-sealed wound.

lake at the lower lid like the temporal wound," he says. "Because the temporal incision sits in that layer of tears, it's easier for the organisms to enter the eye. The superior incision is above the tear lake and, therefore, is sequestered away from the organisms."

Wound Construction

Beyond the location of the incision, the stability of the wound is another important step in preventing endophthalmitis, says Dr. Ernest. The key to proper wound construction is making your incision as square as possible whether you choose the clear corneal, scleral- or limbus-based technique.

Dr. Ernest's research shows that if you construct a square incision in any of these locations, you'll obtain a watertight, stable wound that can withstand external pinpoint pressures up to 525 pounds per square inch. So normal reflexes like rubbing or blinking the eyes won't cause incision leakage and infection.

Other studies show that poorly constructed wounds are a statistically significant risk factor for postop endophthalmitis. In an earlier cadaver model, researchers reported that clear corneal incisions at least 2 mm in length were less likely to develop wound abnormalities such as leaking, gaping, dehiscence and necrosis than shorter incision lengths.⁶

Dr. Ernest makes his wounds 2.75 mm wide by 2.50 mm long. "If the width of your incision is twice as wide as it is long, that's a problem," he says. "Your width relative to your length should be less than 2 to 1. You want mechanical stability before the fibroblasts seal the wound in seven days. If you don't do this, you're setting yourself up for endophthalmitis."

"Wound strength and wound stability are critical," says Dr. Packer, who prefers bimanual phacoemulsification when doing clear corneal incisions that are just anterior to the margin of the limbus. "We're making two incisions that are each 1.2 mm wide, 2.0 mm long and 0.7 mm internally, so that the

A Comprehensive Plan of Prevention

While incision site and wound architecture are critical in the prevention of endophthalmitis, the battle against infection begins with the use of a complex series of sterile techniques administered preoperatively and postoperatively.

William J. Oktavec, MD, an ophthalmologist at San Augustin Eye Foundation in St. Augustine, Fla., says he begins his fight against endophthalmitis by equipping his operating rooms with ultraviolet radiation units that run 24 hours a day. The ultraviolet machines boast electrostatic filters that kill mold and bacteria. They stand 3 feet tall, measure 6 inches wide and conveniently plug into the wall. "The ultraviolet radiation keeps the environment as sterile as possible," says Dr. Oktavec.

A comprehensive course of preop antibiotics is the first line of defense for physicians who don't have ultraviolet radiation units. "My patients use moxifloxacin (Vigamox, Alcon) and gatifloxacin (Zymar, Allergan) eye drops four times a day for three days before surgery," says Dr. Oktavec. "One final drop is instilled in the patient's eyes right before he comes into the surgery center. The rest of the medication is used three to four times a day for 10 days postop."

Ultraviolet lighting systems are also installed in the ORs at St. Luke's Cataract and Laser Institute in Tarpon Springs, Fla. Founder and director James P. Gills, MD, uses ofloxacin (Ocuflox 0.3%, Allergan) preop and postop to ward off infection.

Robert H. Osher, MD, professor of ophthalmology at the University of Cincinnati, and medical director emeritus at the Cincinnati Eye Institute, prefers to give his patients levofloxacin (Quixin, Santen) preop and postop. "Levofloxacin eye drops really give you an outstanding solubility, penetration, safety profile, and broad coverage against gram negative and positive bacteria," he says.

To further reduce the risk of infection, many ophthalmologists routinely use various concentrations of the topical antiseptic povidone iodine in their patients' eyes prior to surgery. It's used to sterilize the surgical field when isolating the eye lashes (a major source of bacteria) with a plastic drape and eyelid speculum. "If you cover the lashes and get them out of the way, you'll have a more sterile and safer surgery," says Dr. Osher. A recent study reported that 5% povidone iodine was more effective at decreasing the conjunctiva bacterial load than the 1% concentration.⁷

Andrew O. Lewicky, MD, assistant professor of ophthalmology at Rush University, and founding partner of Chicago Eye Institute, goes one step further. He instills a 5% concentration of the antiseptic on the cornea and conjunctiva immediately after the surgery. So does Dr. Gills. "Doing this while the patient is still on the table is more effective drop for drop than any antibiotic," says Dr. Lewicky. "I use an anesthetic drop before putting it in the eye, because it does burn."

Following the surgery, Dr. Gills also administers an anterior chamber antibiotic/anti-inflammatory injection for added protection against a wide range of bacteria that may enter the eye.

wound is funnel shaped. We believe that smaller incisions add to the safety of clear corneal surgery and may reduce the rate of endophthalmitis infection."

Dr. Gills keeps the wound "as small as

possible and with as long a bed as possible. For total wound sealing, the corneal bevel should be 2- to 2.5-mm deep and 2.5- to 2.75-mm long," he says. "You have to ask yourself, 'How intact is the


endothelium?' 'Does the cornea act as a trap door to allow bacteria inside the wound?' Endophthalmitis is a direct result of poor wound construction."

While creating a square wound or inserting an IOL, Dr. Donnenfeld warns against making radial tears. "The width of the incision should be as wide as the IOL you insert. You should try to make the incision as small as possible to get the lens in."

Dr. Osher says he produces a tightly sealed near clear corneal incision by making a three-plane construction between 1.5 mm [microphaco] and 3.2 mm in length and dissecting about 2 mm anteriorly. The better the wound construction, the better the prophylaxis, he believes.

The Smaller IOL

The desire to perform cataract surgeries through smaller incisions is spawning new IOL technologies, materials and designs that will allow physicians to insert lenses through incision widths of 1.5 mm or less, says Dr. Packer.

Dr. Gills agrees. "Everyday we try to make cataract surgery a little better than before. And we'll continue to do so as the trend toward smaller incisions continues to grow." 

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