Review Article

Management of corneal perforations: An update

Rashmi Deshmukh, Louis J Stevenson[1], Rasik Vajpayee[1]

Corneal perforation is a potentially devastating complication that can result from numerous conditions that precipitate corneal melting. It is associated with significant morbidity and prompt intervention is necessary to prevent further complications. Causes include microbial keratitis, ocular surface disease, and autoimmune disorders and trauma. Various management options have been described in the literature to facilitate visual rehabilitation. This rview discusses the treatment options that range from temporising measures such as corneal gluing through to corneal transplantation, with decision making guided by the location, size, and underlying aetiology of the perforation.

Key words: Corneal perforation, infective keratitis, sterile corneal melt

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1151_19

Quick Response Code:

Corneal perforation, a potentially devastating complication, can result from numerous conditions that precipitate corneal melting. Numerous causes include microbial keratitis, ocular surface disease, and autoimmune disorders, in addition to trauma where penetrating injuries occur. It is associated with significant ocular morbidity and warrants prompt intervention, both to restore globe integrity and to minimize the risk of secondary complications including endophthalmitis, choroidal hemorrhage, and glaucoma. Various management options have been described in the literature, with multi-staged procedures that are often required to facilitate visual rehabilitation. These procedures range from temporizing measures such as corneal gluing to corneal transplantation, with decision making, guided by the location, size, and underlying etiology of the perforation.

Causes of Corneal Perforation

The causes of corneal perforation can be classified as either traumatic or nontraumatic, with nontraumatic perforation being further divided into infectious or noninfectious causes. Infectious perforation can occur secondary to bacterial, fungal, viral, or parasitic infection while noninfectious etiologies include ocular surface or autoimmune disease. Causative ocular surface conditions include keratoconjunctivitis sicca (KCS) or Sjogren syndrome (SS), while autoimmune conditions leading to perforation include peripheral ulcerative keratitis (PUK) secondary to conditions such as rheumatoid arthritis (RA), Mooren's ulcer, Wegener's granulomatosis, and relapsing polychondritis.[1,2]

Management

Tissue adhesives

Tissue adhesives may be used to manage small corneal perforations. Currently, nonbiologic (cyanoacrylate) and biologic (fibrin glue) adhesives are available.

Cyanoacrylate glue

At present, the following formulations are available for use :

- Indermil (butyl-2-cyanoacrylate; Sherwood, Davis and Geck, St Louis, MO, USA)
- Histoacryl (butyl-2-cyanoacrylate; BBraun, Melsungen, Germany)
- Histoacryl Blue (N-butyl-2-cyanoacrylate; BBraun, Melsungen, Germany)
- Nexacryl (N-butyl-cyanoacrylate; Closure Medical, Raleigh, NC, USA)
- Dermabond (2-octyl-cyanoacrylate; Closure Medical, Raleigh, NC, USA).

Cyanoacrylates are ester derivatives of cyanoacrylic acid. In 1960, Refojo *et al.* first described the technique of treating corneal perforations using cyanoacrylate glue.[3] This method is best suited to perforations that measure less than 3 mm in diameter, are concave in profile, and located away from the limbus. The latter due to the poor adhesion that occurs between the glue and the conjunctival tissue, and the tendency for the adhesive to dislodge when applied in this location.[1,4,5]

Division of Ophthalmology and Visual Sciences, Queens Medical Centre, University of Nottingham, Nottingham, UK, [1]Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia

Correspondence to: Dr. Rashmi Deshmukh, Division of Ophthalmology and Visual Sciences, Eye ENT Centre, Queens Medical Centre, University of Nottingham, Derby Road, Nottingham, NG7 2UH, UK. E-mail: dr.rashmi9@gmail.com

Received: 18-Jun-2019 Revision: 29-Aug-2019
Accepted: 12-Sep-2019 Published: 19-Dec-2019

Cite this article as: Deshmukh R, Stevenson LJ, Vajpayee R. Management of corneal perforations: An update. Indian J Ophthalmol 2020;68:7-14.

Cyanoacrylates undergo polymerization upon contacting water or weak bases, causing them to harden. Short-chain derivatives are strongest, and as such, the tensile strength of N-butyl cyanoacrylate compounds is greater than that of octyl-cyanoacrylates. Dry conditions are required for optimal polymerization of butyl derivatives, with peak bonding strength occurring at 2 min.[3,6]

Derivatives with longer alkyl side chains enjoy the best biocompatibility profile, due to increased production of toxic byproducts that occur with the degradation of shorter alkyl side chain compounds.[7] Similarly, histotoxicity also increases with tissue vascularity.[7] Cyanoacrylates are also bacteriostatic, particularly against gram-positive organisms including *Staphylococcus aureus*, *Streptococcus pneumoniae*, and group A *Streptococci*, an effect that is possibly due to the absence of a lipopolysaccharide capsule among these pathogens.[8] Similarly, the bacteriostatic activity increases with decreasing alkyl side chain length.[9]

Fogle *et al*. demonstrated that the application of cyanoacrylate adhesive to an ulcer bed disrupts stromal melting, in both infective and noninfective cases.[10] Large numbers of polymorphonuclear leucocytes, which have potent collagenolytic and proteolytic activity, are present in active corneal ulcers and promote corneal melting. These leucocytes are stimulated by the interaction between re-epithelializing epithelium and the subjacent keratocytes. Cyanoacrylates inhibit re-epithelialization and consequently inhibit the polymorphonuclear leucocytic infiltration in the diseased area.[11,12]

Techniques of application

While glue can be applied at the slit lamp, it is preferable to perform the procedure in the operating theatre, using the operating microscope under aseptic conditions. Using topical or local anesthesia, an eye speculum is used to gain adequate exposure of the ocular surface, with a noncompressing lid speculum being preferred.

Various techniques have described the effective application of cyanoacrylate adhesive to corneal perforations. The glue can be drawn into a syringe using a 20G needle, before being applied as a drop to the corneal defect using a 27G or 30G cannula. This allows a small amount of glue to be applied in a controlled manner. The application of glue must be performed rapidly to avoid polymerization and hardening of the glue in the cannula.[13] Once in contact with the cornea, the glue spreads to cover the perforation, forming a hardened seal within a few seconds. Additional glue can then be applied as needed in the event of a persistent leak. Following this, a bandage contact lens (BCL) is used to cover the site.[14,15] The adherence of the glue, and thus the success of the procedure, can be improved by ensuring that the site of gluing is debrided of necrotic epithelium beforehand and kept dry throughout the procedure.[14]

In cases where the iris tissue plugs the perforation or where the anterior chamber collapses, it is advisable that the anterior chamber is reformed using viscoelastic material or an air bubble to prevent contact between the glue and intraocular structures.[14,16]

Moreover, an alternate method of utilizing a disc made out of sterile plastic drape to apply the glue, has also been described, wherein, a disc of drape is cut and a drop of glue is placed on it. The disc is then placed over the perforation, and the glue is allowed to dry before a BCL is inserted.[17] This gives the adhesive a smoother surface to adhere to and prevents the inadvertent instillation of glue into the anterior chamber.

A modified version of this technique, as described by Khalifa *et al*., involves gluing a disc of sterile plastic drape over the perforation using cyanoacrylate, similar to a tectonic patch. This has the advantage of avoiding direct contact between the glue and anterior chamber thus, limiting any potential immune response elicited by the glue.[17] In an attempt to glue defects larger than 3 mm, a number of other modified techniques have been described. Moschos *et al.* described using a 10–0 nylon suture, placed as a mesh across the defect, over which the glue is applied[18] while Gandhewar *et al.* described placing a double layer of sterile plastic drape between the glue and the anterior chamber to form a barrier which bridges the defect site.[19]

Regardless of the technique of application, the eye must be closely examined after gluing to ensure that no leaks are present, and that reformation of the anterior chamber occurs [Fig. 1a and b]. However, in most cases, the glue patch only temporarily occludes the perforation; and during this time wound healing has the opportunity to occur.[20] Nevertheless, the literature reports this to be an effective method for managing small perforations, the outcomes following gluing may vary in different studies.[21,22] In one series, Setlik *et al.* reported that over 40% of cases healed following the use of tissue adhesive alone while Hirst *et al.* reported both lower enucleation rates and improved visual outcomes with the use of tissue adhesives.[23]

Complications and adverse effects

The primary concern regarding cyanoacrylate use is its stromal, endothelial, and lenticular toxicity when directly contacting the cornea or lens.[24,25] One difficulty with accurately quantifying the toxic effects of cyanoacrylate is delineating the effects of the glue versus the underlying disease process. Other complications can include raised intraocular pressure, possibly secondary to inflammation affecting the trabecular meshwork, (1) and microbial keratitis, especially with prolonged use.[26,27] Moreover, it is uncertain if the latter is due to the glue itself, given that it has antimicrobial properties, or due to the presence of a BCL. As such, close observation of patients is essential, particularly those who are immunocompromised.[18] It is hoped, that as newer derivatives with longer alkyl side chains are developed, the biocompatibility of cyanoacrylate glue improves, leading to fewer adverse effects.[26]

Fibrin glue

Fibrin glue is a biologic product containing fibrinogen and thrombin. It is completely biodegradable and induces minimal stromal inflammation or tissue necrosis,[28] therefore, less toxic than cyanoacrylate, providing a more suitable environment for healing.[29] In general, thrombin catalyzes the conversion of fibrinogen to fibrin in the coagulation pathway, resulting in the formation of a hemostatic plug. When applied to a corneal perforation, this hemostatic plug forms an effective sealant, and when used for defects up to 2 mm is as effective as cyanoacrylate.[30,31] However, for defects between 2–3 mm, cyanoacrylate appears to be superior.[32] Due to its role in the coagulation pathway, fibrin plays an integral role in wound healing. Intrinsically, it enhances scar tissue formation when used for corneal perforations and is associated with a reduced incidence of corneal vascularization and giant

papillary conjunctivitis.[32,33] However, in particular, fibrin glue degrades more quickly than cyanoacrylate glue, does not have antibacterial properties, and bovine-derived products may transmit prion or viral disease.[8,29,34]

Conjunctival flaps

Superior forniceal conjunctival advancement pedicels, such as Gundersen or Cies's racquet conjunctival flap, are typically used for indolent, nonhealing, corneal ulcers, and impending perforations.[35] These flaps require extensive conjunctival dissection and obscure the cornea postoperatively. They promote extensive corneal vascularization which facilitates corneal healing[36,37] but simultaneously increases the risk of graft rejection if one is performed at a later stage.

As suggested by the name, a superior forniceal conjunctival flap is mobilized on a pedicle and transferred to cover the defect. This biological patch provides trophic factors, mechanically protects the cornea, and offers analgesic effects. In addition to corneal vascularization, complications include, flap perforation or fenestration, and partial or complete flap displacement, particularly when managing central lesions.[38]

Amniotic membrane transplant

In 1997, Lee and Tseng were the first to propose the use of amniotic membrane transplantation (AMT) for the treatment of corneal epithelial defects.[39] Chen *et al*. subsequently reported the effectiveness of AMT in severe neurotrophic keratopathy[40] and studies have since described the successful use of AMT in the management of corneal perforations.[41-43] The technique allows rapid restoration of corneal integrity, avoiding the need for urgent keratoplasty.[44]

AMT is particularly useful in cases of central perforation where conjunctival flaps have a greater risk of displacement. Furthermore, conjunctival flaps used in large perforations carry an increased risk of nonadherence to the cornea, resulting in hypotony and predisposing the eye to endophthalmitis. AMT also induces less vascularization than conjunctival flaps, increasing the chance of successful keratoplasty in the future.[45]

Properties of amniotic membrane

Amniotic membrane has several properties that make it suited for use in the management of corneal perforations. Amniotic membrane epithelium contains growth factors including hepatocyte growth factor, keratocyte growth factor, and epidermal growth factor. The presence of these trophic factors aid epithelial healing by promoting differentiation and migration of epithelial cells that are in contact with the amniotic membrane.[46-48] Inhibitory proteases released by the amniotic membrane also induce apoptosis of local inflammatory cells, reducing the risk of corneal melt.[49] Reports have also suggested that stromal tissue is synthesized from the amniotic membrane in cases involving deep ulcers or descemtocoeles.[41]

Surgical technique and outcomes

Multilayered AMT is preferred in the management of deep corneal ulcers or perforations. This involves filling the defect with multiple pieces of amniotic membrane before covering the entire cornea with a final layer of transplanted tissue.[44,50] The transplanted membrane can then be secured using sutures or fibrin glue.[43] Using this technique, Rodríguez-Ares *et al.* reported a 100% healing rate for micro-perforations and an almost 75% rate of closure for perforations up to 1.5 mm in diameter.[45] AMT in combination with fibrin glue has also been demonstrated to be effective at managing defects up to 3 mm in size,[51] while piled, multilayered AMT, forming an augmented patch has been used in combination with fibrin glue to treat defects greater than 3 mm.[5]

Tenon's patch graft

The use of Tenon's capsule has been described in the repair of traumatic scleral perforations and leaking trabeculectomy blebs.[52] Recently, the use of a Tenon's patch graft has been described in the management of large corneal perforations, measuring up to 6 mm, where tissue adhesive is not suitable.[53] Anatomically, Tenon's capsule arises 2 mm posterior to the limbus, and it is postulated in such a way that it has the ability to produce autologous fibroblasts and connective tissue, allowing it to be incorporated into the host's corneal tissue.[53,54]

Harvesting the Tenon's graft

Incisions are made posterior to the scleral insertion of Tenon's capsule, in the inferotemporal and inferonasal quadrant, and a portion of the capsule excised. It is advised that the size of the graft is slightly larger than the size of the corneal defect. The site of harvest can simultaneously be used to drain choroidal effusions, which may be present in cases where a large perforation is present.[53,55]

Applying the Tenon's patch graft

Before applying the graft, the cornea is debrided, removing debris, and the epithelium adjacent to the perforation. The graft is then ironed into a thin layer and placed over the defect before being secured in place using either tissue adhesive or sutures. Following this, the anterior chamber is reformed using an air bubble, with the fluid being avoided during this process to reduce the risk of malignant glaucoma. As healing occurs, the Tenon's graft is incorporated into the corneal scar and the success of this procedure is up by 75%, as reported by Korah *et al*. [Fig. 2a and b].[53]

Advantages

Tenon's capsule is an autologous transplant, hence no immune response is evoked and thus tissue rejection does not occur. Furthermore, unlike corneal grafting or AMT, this tissue does not rely on donor tissue or it's associated infrastructure such as eye banks, and thus supply can be more readily guaranteed. Lastly, as there are no heterologous antigenic sensitization, corneal grafting is more likely to succeed if performed at a later stage.

Keratoplasty procedures

Large corneal perforations are not amenable to the abovementioned treatment modalities and often require a tectonic keratoplasty. Tectonic corneal transplants restore globe integrity by filling corneal stromal defects. Surgical techniques such as full-thickness keratoplasty, lamellar keratoplasty, and corneal patch grafts have been described, and are chosen depending on the size, depth, location, and cause of perforation.[56,57] In recent years, lamellar keratoplasties have become increasingly popular owing to the lower rate of graft rejection compared to penetrating keratoplasty (PK).

Corneal perforations secondary to infective keratitis

Therapeutic keratoplasty not only restores the integrity of the globe but also reduces the microbial and necrotic tissue load, and thus reduces the associated toxins and enzymes which contribute to the progression of infective keratitis and corneal

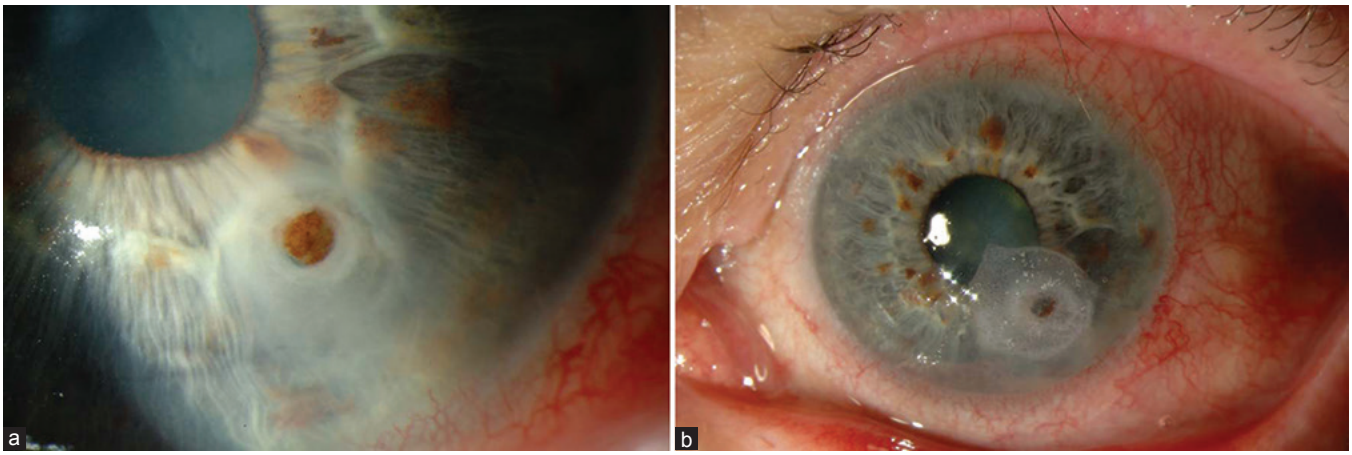

Figure 1: (a) Small corneal perforation prior to the application of glue (b) Corneal perforation sealed using cyanoacrylate glue

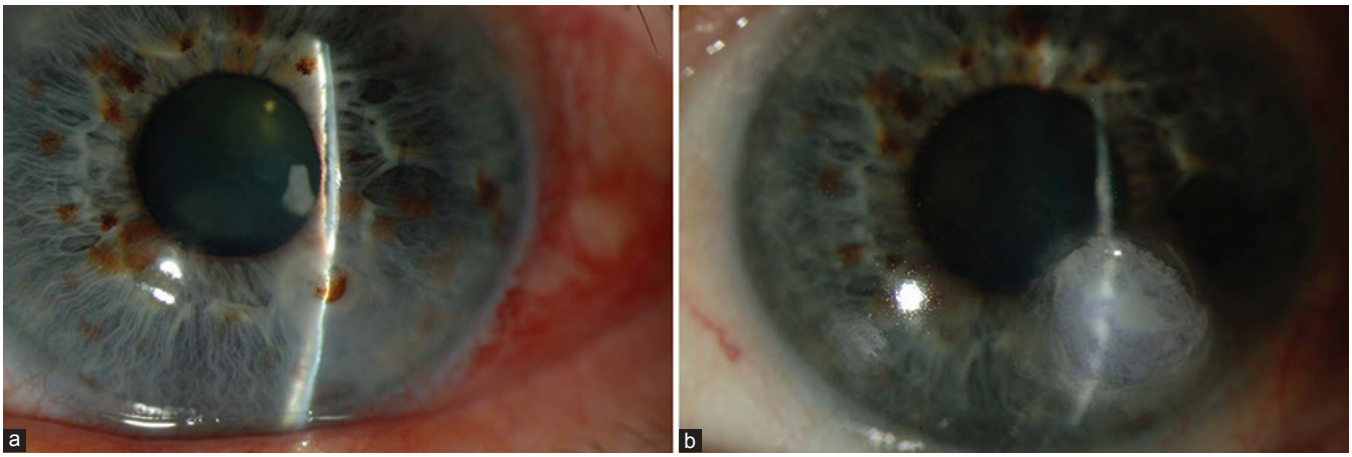

Figure 2: (a) Corneal perforation prior to application of Tenon's patch graft (b) Corneal perforation successfully sealed using a Tenon's patch graft, secured using glue

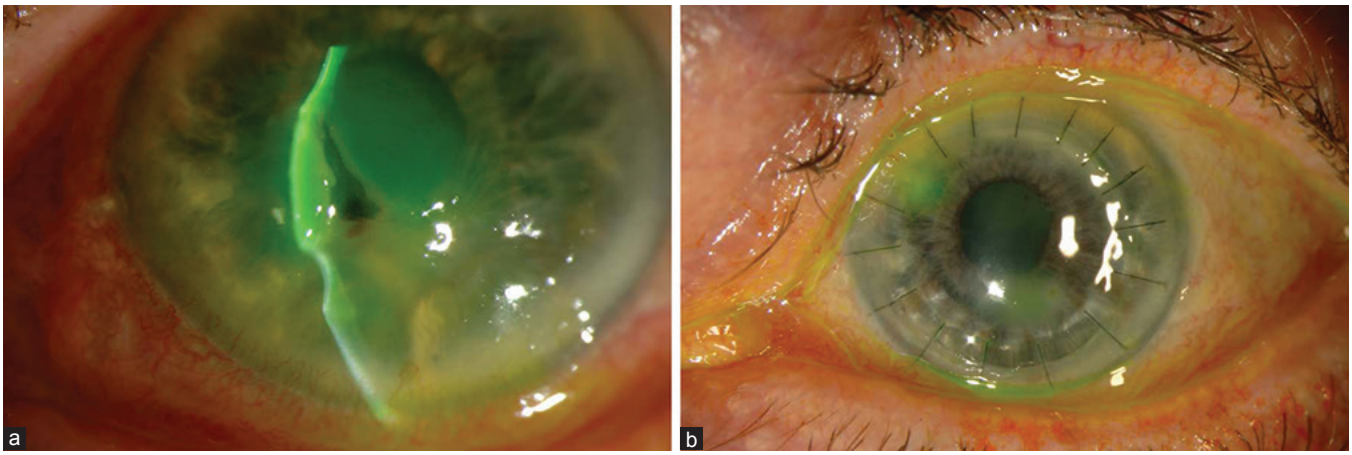

Figure 3: (a) Corneal perforation secondary to herpes simplex viral (HSV) keratitis (b) Corneal perforation secondary to herpes simplex viral (HSV) keratitis managed using a lamellar keratoplasty

stromal melt. The ideal timing of the surgery varies significantly among the patients. Where the anterior chamber is flat, it is recommended that grafting needs to be performed within 24-48 hours, to minimize long-term complications.[58] However, Nobe *et al.* reported improved graft survival in cases where keratoplasty was delayed, suggesting that where the anterior chamber is maintained, this approach should be pursued.[59] Tectonic epikeratoplasty, typically used in the management of sterile corneal melt, has also been used in the management of infectious keratitis. However, Bull *et al.* concluded that this procedure was inferior to that of penetrating keratoplasty in the above context.[60]

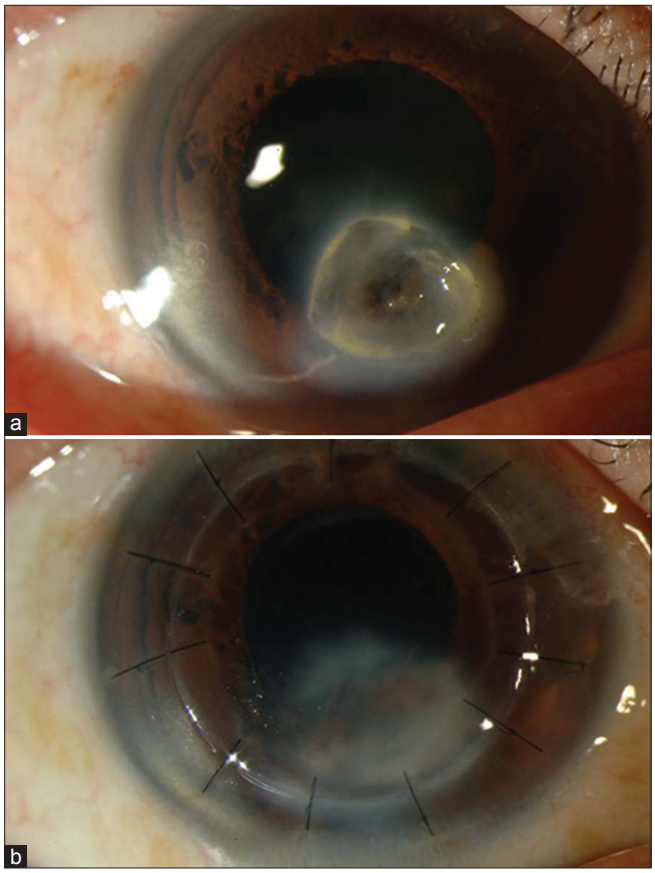

Figure 4: (a) Corneal perforation with iridocorneal adhesion (b) Corneal perforation with iridocorneal adhesion managed using lamellar keratoplasty, allowing for iris preservation

The trephination of host tissue is technically difficult in the absence of tissue rigidity and, as such, a Flieringa ring may be needed to provide scleral support intraoperatively. All necrotic tissue should be excised with a 1 mm margin of healthy tissue, to ensure a healthy donor bed free of infection. A superficial mark is made with a trephine and used as a guide to excise the diseased corneal tissue. Once the tissue is excised, anterior and posterior synechiae are gently lysed before suturing the donor cornea in place [Fig. 3a and b].

Corneal perforation with iris plugging

It is not uncommon for the iris tissue to plug a perforation and form a pseudocornea. The presence of iridocorneal adhesions increases the chances of iris tissue avulsion and hemorrhage during surgery. This results as the removal of adherent corneal tissue requires a greater force than the iris tissue can withstand, leading to iris tears and bleeding. Vajpayee *et al.* described a technique of lamellar separation for such cases involving initial debulking of the cornea using lamellar dissection, followed by entry into the anterior chamber. This allows gentle separation of the deep corneal lamellae from the adherent iris tissue, helping to preserve iris tissue and reduce the risk of subsequent complications including anterior synechiae, secondary glaucoma, and iris defects, in turn, improving graft survival [Fig. 4a and b].[61]

Corneal perforations in sterile melts

Tectonic epikeratoplasty (TEK) is a procedure that has been described in the management of sterile corneal melts [Fig. 5]. In this procedure, donor corneal tissue is placed over the perforated cornea and sutured to the surrounding sclera after a 360° peritomy has been performed. It is then left in place to allow the underlying site of stromal melt to heal.[62] Donor corneas that are unsuitable for use as an optical graft owing to poor endothelial cell count or stromal scarring may be used for this purpose, giving this procedure an advantage from a healthy resource perspective. Similarly, Lazaridis *et al.* used ethanol-preserved donor corneal stroma, derived as a by-product following endothelial keratoplasty graft preparation, and reported good outcomes.[62]

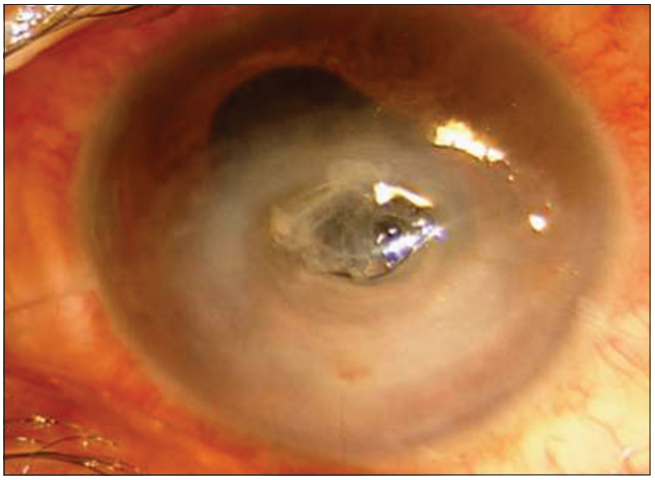

Figure 5: Corneal perforation in a neurotrophic cornea

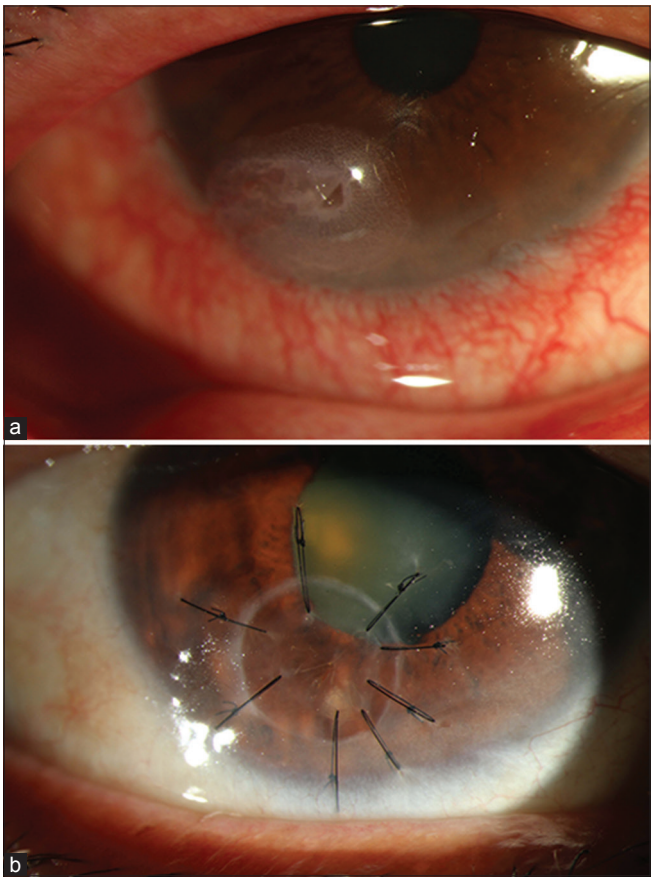

Figure 6: (a) Peripheral corneal perforation (b) Peripheral corneal perforation managed using a tectonic patch graft

As described by Paufique in 1950, lamellar corneal patch grafting can also be used in the management of corneal perforations and descemetocoeles.[63,64] Sutured corneal patch grafts [Fig. 6a and b] offer greater structural integrity compared to tissue adhesives in cases of large perforations and are visually less disabling than cyanoacrylate glue in central perforations. Patch grafting also removes necrotic tissue that itself is a source of collagenases and drives stromal melting.[8]

The use of glycerol-preserved corneas for patch grafts has also been described.[65] Chu *et al.* used corneas preserved in Optisol-GS and reported favorable results.[66] In this study, donor corneal tissue, remaining after lenticule preparation for descemet-stripping automated endothelial keratoplasty (DSAEK), was used. Similarly, Bhandari *et al.* used lenticules extracted during small incision lenticule extraction (SMILE) for micro-perforations in seven patients and reported successful results at 3 months postoperatively.[67] Jiang *et al.* conducted a similar study with SMILE lenticules and followed up 22 eyes for 6 months, with globe integrity achieved in all cases in their series.[68]

Peripheral corneal perforations

Several procedures have been described for dealing with peripheral perforations and corneal thinning disorders.

Corneal wedge resection

As described in the management of pellucid marginal degeneration (PMD), this technique involves excising the cornea in the region of peripheral thinning, before filling the resultant defect with a segment of healthy donor corneal tissue.[69] It is effective in patients with small areas of corneal thinning where sutures do not affect the visual axis.[70] Common complications include loose sutures, vascularization, and against-the-rule astigmatism.[71]

Crescentic lamellar keratoplasty

This procedure is used in cases where there is significant peripheral thinning such as Terrien's marginal degeneration (TMD) or Mooren's ulcer.[72] After preparing the host bed, a ring-shaped lamellar graft is sutured to the peripheral cornea. Moreover, successful surgery using both cryopreserved and glycerin-preserved tissue has been reported.[73]

Copy and fix technique

The copy and fix technique for peripheral corneal perforations involves marking the area to be excised on the host cornea with a marking pen. The donor corneoscleral rim is placed over the marked area and the exact shape is traced on it. The graft is then harvested along the marked lines and fixed in place with sutures.[74]

Other procedures

Other procedures including tuck-in lamellar keratoplasty, large penetrating keratoplasty, and corneoscleroplasty have additionally been described in the management of peripheral perforations.[70]

Future directions

Corneal perforations and subsequent scarring are a major cause of corneal blindness worldwide. A shortage of donor corneas available for transplantation has prompted research into the production and use of bioengineered tissue. Collagen is a biocompatible and biodegradable substrate that has been used to fabricate artificial corneal tissue.[75] However, owing to the highly hydrated nature of collagen, collagen-based hydrogels are structurally weak and difficult to manipulate.[76] While compressing collagen hydrogels ensures to improve their mechanical properties, these materials are still too weak for clinical use.[77] Thus, plastic compressed gels and electrospun constructs have been developed to overcome this issue with promising results.[78]

Conclusion

The management of a corneal perforation depends on the size, shape, location, and cause of the lesion. Smaller lesions may be managed with tissue adhesives, Tenon's patch grafting, or amniotic membrane transplantation. Larger perforations, however, may need urgent keratoplasty. Ongoing advances are being made towards the use of lamellar corneal tissue to reduce the rate of rejection and improve clinical outcomes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lekskul M, Fracht HU, Cohen EJ, Rapuano CJ, Laibson PR. Nontraumatic corneal perforation. Cornea 2000;19:313-9.
2. Jhanji V, Young AL, Mehta JS, Sharma N, Agarwal T, Vajpayee RB. Management of corneal perforation. Surv Ophthalmol 2011;56:522-38.
3. Refojo MF, Dohlman CH, Ahmad B, Carroll JM, Allen JC. Evaluation of adhesives for corneal surgery. Arch Ophthalmol 1968;80:645-56.
4. Grinstaff MW. Designing hydrogel adhesives for corneal wound repair. Biomaterials 2007;28:5205-14.
5. Kim HK, Park HS. Fibrin glue-assisted augmented amniotic membrane transplantation for the treatment of large noninfectious corneal perforations. Cornea 2009;28:170-6.
6. Refojo MF, Dohlman CH. The tensile strength of adhesive joints between eye tissues and alloplastic materials. Am J Ophthalmol 1969;68:248-55.
7. Trott AT. Cyanoacrylate tissue adhesives: An advance in wound care. JAMA 1997;277:1559-60.
8. Eiferman RA, Snyder JW. Antibacterial effect of cyanoacrylate glue. Arch Ophthalmol 1983;101:958-60.
9. Lehman RA, West RL, Leonard F. Toxicity of alkyl 2-cyanoacrylates: II. Bacterial growth. Arch Surg 1966;93:447-50.
10. Fogle J, Kenyon KR, Foster CS. Tissue adhesive arrests stromal melting in the human cornea. Am J Ophthalmol 1980;89:795-802.
11. Kiyoo N. Interaction between corneal invasion of polymorphonuclear leukocytes and corneal epithelium. Nippon Ganka Gakkai Zasshi 1990;94:445-56.
12. Dohlman CH, Refojo MF, Carrol J, Gasset A. Artificial corneal epithelium. Arch Ophthalmol 1968;79:360.
13. Gavin EA, Mahroo OA, Lim R, de Benito-Llopis L. Using cyanoacrylate glue for corneal perforations: Caution with use of a needle and syringe. Cornea 2013;32:e193.
14. Portnoy SL, Insler MS, Kaufman HE. Surgical management of corneal ulceration and perforation. Surv Ophthalmol 1989;34:47-58.
15. Rana M, Savant V. A brief review of techniques used to seal corneal perforation using cyanoacrylate tissue adhesive. Cont Lens Anterior Eye 2013;36:156-8.
16. Hirst LW, Stark W, Jensen AD. Tissue adhesives: New perspectives in corneal perforations. Ophthalmic Surg 1979;10:58-64.

17. Vote BJ, Elder MJ. Cyanoacrylate glue for corneal perforations: A description of a surgical technique and a review of the literature. Clin Exp Ophthalmol 2000;28:437-42.
18. Moschos M, Droutsas D, Boussalis P, Tsioulias G. Clinical experience with cyanoacrylate tissue adhesive. Doc Ophthalmol 1997;93:237-45.
19. Gandhewar J, Savant V, Prydal J, Dua H. Double drape tectonic patch with cyanoacrylate glue in the management of corneal perforation with iris incarceration. Cornea 2013;32:e137-8.
20. Webster RG, Slansky HH, Refojo MF, Boruchoff SA, Dohlman CH. The use of adhesive for the closure of corneal perforations: Report of two cases. Arch Ophthalmol 1968;80:705-9.
21. Setlik DE, Seldomridge DL, Adelman RA, Semchyshyn TM, Afshari NA. The effectiveness of isobutyl cyanoacrylate tissue adhesive for the treatment of corneal perforations. Am J Ophthalmol 2005;140:920-1.
22. Moorthy S, Jhanji V, Constantinou M, Beltz J, Graue-Hernandez EO, Vajpayee RB. Clinical experience with N-butyl cyanoacrylate tissue adhesive in corneal perforations secondary to herpetic keratitis. Cornea 2010;29:971-5.
23. Hirst LW, Smiddy WE, Stark WJ. Corneal perforations: Changing methods of treatment, 1960-1980. Ophthalmology 1982;89:630-5.
24. Golubović S, Parunović A. Cyanoacrylate glue in the treatment of corneal ulcerations. Fortschr Ophthalmol 1990;87:378-81.
25. Lehman RA, Hayes GJ, Leonard F. Toxicity of alkyl 2-cyanoacrylates: I. Peripheral nerve. Arch Surg 1966;93:441-6.
26. Weiss JL, Williams P, Lindstrom RL, Doughman DJ. The use of tissue adhesive in corneal perforations. Ophthalmology 1983;90:610-5.
27. Leahey AB, Gottsch JD, Stark WJ. Clinical experience with N-butyl cyanoacryiate (Nexacryl) tissue adhesive. Ophthalmology 1993;100:173-80.
28. Radosevich M, Goubran H, Burnouf T. Fibrin sealant: Scientific rationale, production methods, properties, and current clinical use. Vox Sang 1997;72:133-43.
29. Chen WL, Lin CT, Hsieh CY, Tu IH, Chen WY, Hu FR. Comparison of the bacteriostatic effects, corneal cytotoxicity, and the ability to seal corneal incisions among three different tissue adhesives. Cornea 2007;26:1228-34.
30. Lagoutte F, Gauthier L, Comte P. A fibrin sealant for perforated and preperforated corneal ulcers. Br J Ophthalmol 1989;73:757-61.
31. Scalcione C, Ortiz-Vaquerizas D, Said D, Dua H. Fibrin glue as agent for sealing corneal and conjunctival wound leaks. Eye 2018;32:463-6.
32. Siatiri H, Moghimi S, Malihi M, Khodabande A. Use of sealant (HFG) in corneal perforations. Cornea 2008;27:988-91.
33. Sharma A, Kaur R, Kumar S, Gupta P, Pandav S, Patnaik B, *et al*. Fibrin glue versus N-butyl-2-cyanoacrylate in corneal perforations. Ophthalmology 2003;110:291-8.
34. Sii F, Lee GA. Fibrin glue in the management of corneal melt. Clin Exp Ophthalmol 2005;33:532-4.
35. Sandinha T, Zaher S, Roberts F, Devlin H, Dhillon B, Ramaesh K. Superior forniceal conjunctival advancement pedicles (SFCAP) in the management of acute and impending corneal perforations. Eye 2006;20:84-9.
36. Gundersen T. Conjunctival flaps in the treatment of corneal disease with reference to a new technique of application. AMA Arch Ophthalmol 1958;60:880-8.
37. Cies WA, Odeh-Nasrala N. The racquet conjunctival flap. Ophthalmic Surg Lasers Imaging Retina 1976;7:31-2.
38. Gundersen T, Pearlson H. Conjunctival flaps for corneal disease: Their usefulness and complications. Trans Am Ophthalmol Soc 1969;67:78-95.
39. Lee SH, Tseng SC. Amniotic membrane transplantation for persistent epithelial defects with ulceration. Am J Ophthalmol 1997;123:303-12.
40. Chen H-J, Pires RT, Tseng SC. Amniotic membrane transplantation for severe neurotrophic corneal ulcers. Br J Ophthalmol 2000;84:826-33.
41. Solomon A, Meller D, Prabhasawat P, John T, Espana EM, Steuhl KP, *et al*. Amniotic membrane grafts for nontraumatic corneal perforations, descemetoceles, and deep ulcers. Ophthalmology 2002;109:694-703.
42. Duchesne B, Tahi H, Galand A. Use of human fibrin glue and amniotic membrane transplant in corneal perforation. Cornea 2001;20:230-2.
43. Su CY, Lin CP. Combined use of an amniotic membrane and tissue adhesive in treating corneal perforation: A case report. Ophthalmic Surg Lasers Imaging Retina 2000;31:151-4.
44. Prabhasawat P, Tesavibul N, Komolsuradej W. Single and multilayer amniotic membrane transplantation for persistent corneal epithelial defect with and without stromal thinning and perforation. Br J Ophthalmol 2001;85:1455-63.
45. Rodríguez-Ares MT, Touriño R, López-Valladares MJ, Gude F. Multilayer amniotic membrane transplantation in the treatment of corneal perforations. Cornea 2004;23:577-83.
46. Kilby M, Afford S, Li X, Strain A, Ahmed A, Whittle M. Localisation of hepatocyte growth factor and its receptor (c-met) protein and mRNA in human term placenta. Growth Factors 1996;13:133-9.
47. Sotozono C, Kinoshita S, Kita M, Imanishi J. Paracrine role of keratinocyte growth factor in rabbit corneal epithelial cell growth. Exp Eye Res 1994;59:385-91.
48. Kurpakus MA, Stock EL, Jones JC. The role of the basement membrane in differential expression of keratin proteins in epithelial cells. Dev Biol 1992;150:243-55.
49. Boudreau N, Werb Z, Bissell MJ. Suppression of apoptosis by basement membrane requires three-dimensional tissue organization and withdrawal from the cell cycle. Proc Nat Acad Sci 1996;93:3509-13.
50. Hanada K, Shimazaki J, Shimmura S, Tsubota K. Multilayered amniotic membrane transplantation for severe ulceration of the cornea and sclera. Am J Ophthalmol 2001;131:324-31.
51. Hick S, Demers PE, Brunette I, La C, Mabon M, Duchesne B. Amniotic membrane transplantation and fibrin glue in the management of corneal ulcers and perforations: A review of 33 cases. Cornea 2005;24:369-77.
52. Morris DA, Ramocki JM, Shin DH, Glover BK, Kim YY. Use of autologous Tenon's capsule and scleral patch grafts for repair of excessively draining fistulas with leaking filtering blebs. J Glaucoma 1998;7:417-9.
53. Korah S, Selvin SS, Pradhan ZS, Jacob P, Kuriakose T. Tenons patch graft in the management of large corneal perforations. Cornea 2016;35:696-9.
54. Kakizaki H, Takahashi Y, Nakano T, Asamoto K, Ikeda H, Ichinose A, *et al*. Anatomy of Tenons capsule. Clin Exp Ophthalmol 2012;40:611-6.
55. Singh R, Umapathy T, Abedin A, Eatamadi H, Maharajan S, Dua HS. Choroidal detachment in perforated corneal ulcers: Frequency and management. Br J Ophthalmol 2006;90:1111-4.
56. Cowden JW, Copeland RA, Schneider MS. Large diameter therapeutic penetrating keratoplasties. Refract Corneal Surg 1989;5:244-8.
57. Ang M, Mehta JS, Arundhati A, Tan DT. Anterior lamellar keratoplasty over penetrating keratoplasty for optical, therapeutic, and tectonic indications: A case series. Am J Ophthalmol 2009;147:697-702.e2.
58. Stamate AC, Tătaru CP, Zemba M. Emergency penetrating keratoplasty in corneal perforations. Rom J Ophthalmol 2018;62:253-9.
59. Nobe JR, Moura BT, Robin JB, Smith RE. Results of penetrating keratoplasty for the treatment of corneal perforations. Arch Ophthalmol 1990;108:939-41.
60. Bull H, Behrens-Baumann W. [Tectonic epikeratoplasty as an

alternative to keratoplasty a chaud?]. Klin Monbl Augenheilkd 1997;210:78-81.

61. Vajpayee RB, Singhvi A, Sharma N, Sinha R. Penetrating keratoplasty for perforated corneal ulcers: Preservation of iris by corneal debulking. Cornea 2006;25:44-6.
62. Machowicz-Matejko E, Rakowska E, Zagorski Z. Results of tectonic epikeratoplasty in the management of corneal perforations. Klin Oczna 2010;112:296-300.
63. Paufique L, Philps S. Acute eye lesions treated by lamellar corneal grafting. Br J Ophthalmol 1950;34:746-8.
64. Paufique L. Indications for the therapeutic lamellar corneal graft. Am J Ophthalmol 1950;33:24.
65. Lin HC, Ong SJ, Chao AN. Eye preservation tectonic graft using glycerol-preserved donor cornea. Eye 2012;26:1446-50.
66. Chu HS, Hsieh MC, Chen YM, Hou YC, Hu FR, Chen WL. Anterior corneal buttons from DSAEK donor tissue can be stored in optisol GS for later use in tectonic lamellar patch grafting. Cornea 2014;33:555-8.
67. Bhandari V, Ganesh S, Brar S, Pandey R. Application of the SMILE-derived glued lenticule patch graft in microperforations and partial-thickness corneal defects. Cornea 2016;35:408-12.
68. Jiang Y, Li Y, Liu X-W, Xu J. A novel tectonic keratoplasty with femtosecond laser intrastromal lenticule for corneal ulcer and perforation. Chin Med J 2016;129:1817-21.
69. Cameron JA. Results of lamellar crescentic resection for pellucid marginal corneal degeneration. Am J Ophthalmol 1992;113:296-302.
70. Lohchab M, Prakash G, Arora T, Maharana P, Jhanji V, Sharma N, *et al*. Surgical management of peripheral corneal thinning disorders. Surv Ophthalmol 2019;64:67-78.
71. Maccheron LJ, Daya SM. Wedge resection and lamellar dissection for pellucid marginal degeneration. Cornea 2012;31:708-15.
72. Li L, Zhai H, Xie L, Cheng J, Liu W. Therapeutic effects of lamellar keratoplasty on terrien marginal degeneration. Cornea 2018;37:318-25.
73. Li J, Shi S, Zhang X, Ni S, Wang Y, Curcio CA, *et al*. Comparison of different methods of glycerol preservation for deep anterior lamellar keratoplasty eligible corneas. Invest Ophthalmol Vis Sci 2012;53:5675-85.
74. Samarawickrama C, Goh R, Vajpayee RB. "Copy and Fix": A new technique of harvesting freehand and horseshoe tectonic grafts. Cornea 2015;34:1519-22.
75. Liu D, Nikoo M, Boran G, Zhou P, Regenstein JM. Collagen and gelatin. Annu Rev Food Sci Technol 2015;6:527-7.
76. Jiang Q, Reddy N, Zhang S, Roscioli N, Yang Y. Water-stable electrospun collagen fibers from a non-toxic solvent and crosslinking system. J Biomed Mater Res A 2013;101:1237-47.
77. Mi S, Connon CJ. The formation of a tissue-engineered cornea using plastically compressed collagen scaffolds and limbal stem cells. Methods Mol Biol 2013;1014:143-55.
78. Barnes CP, Sell SA, Boland ED, Simpson DG, Bowlin GL. Nanofiber technology: Designing the next generation of tissue engineering scaffolds. Adv Drug Deliv Rev 2007;59:1413-33.

Know the Authors

Dr Rashmi Deshmukh

Rashmi Deshmukh was trained in ophthalmology at JIPMER, Pondicherry, where she received the Best Resident Gold Medal. She pursued RGUHS-accredited Cornea and Refractive Surgery fellowship at Narayana Nethralaya, Bangalore, under the mentorship of Dr Rohit Shetty, where she was part of several path-breaking studies that brought her several accolades. She was a faculty on the Cornea Service at Centre for Sight, New Delhi for two years, and is currently a cornea fellow at the University of Nottingham, UK under the preceptorship of Prof Harminder S Dua. She is the recipient of IJO Honour Award for Peer Review 2019, IJO Silver Award for an outstanding publication 2019, Best Paper APACRS 2017, Travel Grant ARVO 2017, KC Singhal Best Paper AIOS 2017, Best Paper APACRS 2016, and Best Paper KOS 2016. Rashmi has published about 20 peer-reviewed manuscripts and is currently the Assistant Editor of Indian IJO.

Dr Louis Stevenson

Louis Stevenson is a junior doctor currently working with Lions Outback Vision. This organisation provides ophthalmology services to remote Western Australia, using a mobile clinic to travel between population centres. This has allowed patients to access specialist eye care in regions where this was previously not possible. In 2020, Louis is moving to Melbourne, Australia to commence ophthalmology training at the Royal Victorian Eye and Ear Hospital.

Prof Rasik Vajpayee

Rasik Vajpayee is one of the world's leading experts in the field of corneal and cataract surgery. He has been the Head of Corneal, Cataract and Refractive Surgery units of the Dr Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi (1998-2013) and of Royal Victorian Eye and Ear Hospital, Melbourne, Australia (2006-2011). Besides innovating many cataract and corneal surgery techniques, he has pioneered the use of single donor cornea for multiple patients. He is the recipient of a number of awards around the world, including several orations and fellowships and has published/edited 14 books, and more than 365 research papers.