In the swamp lands of Louisiana the dead are buried in tombs above ground rather than interred in the waterlogged earth. Observation of this reversal of the usual arrangements prompted TP Werblin to conceive the procedure of epikeratophakia in 1979. In this keratorefractive technique, instead of attempting direct invasive modification of the corneal contour, a preshaped refractive lamella is simply placed on top of the existing corneal structure (fig 8.1).

The refractive lamella or "lenticule" that is used in epikeratophakia can be prepared before the operation. Ophthalmic surgeons may choose to prepare the corneal tissue themselves and there is a variety of techniques available for this. Alternatively, the lenticule can be obtained from a central manufacturing source, so freeing the surgeon from this time consuming and technically demanding task.

Full thickness donor tissue is used to prepare the lenticule and a wide range of dioptic power can be incorporated, such that the full range of spherical refractive errors from high myopia to high hypermetropia can be corrected (fig 8.2). In addition, a lenticule of plano power can be used to modify the abnormal corneal shape.
Epikeratophakia for myopia: the graft produces a flatter anterior corneal curvature in the central optic zone.

found in keratoconus and restore a normal contour, with reduction of the coexisting myopia and astigmatism (fig 8.3).

The surgical procedure involves removal of the host corneal epithelium and fixation of the edge of the donor tissue into an annular bed. After the operation, the host epithelium will grow over the donor tissue, and with time the host keratocytes migrate into the lenticule stroma. The donor tissue thus becomes what has been termed a "living contact lens".

Although there is wound healing between the periphery of the lenticule and the host stroma, there is no bonding of the posterior surface of the lenticule to the host Bowman's layer. For this reason it is possible to remove an epikeratophakia lenticule, and the host Bowman's layer will subsequently become rapidly re-epithelialised. Its potential reversibility places epikeratophakia in a completely different category from virtually all other refractive surgical procedures, and often makes it the procedure of choice where there is any doubt about the overall risk/benefit ratio of refractive surgery. In retrospect it is remarkable that such a simple and elegant concept had remained elusive for so many years.
Keratomileusis and keratophakia

The requisite technology to shape a refractive lamella from corneal tissue—the cryolathe—had been devised some 40 years earlier by Barraquer in Columbia. Barraquer’s methods of keratorefractive surgery required direct excision of a lamella of the patient’s cornea with a miniature motorised plane—the microkeratome—and this excised lamella was subsequently modified in shape on the cryolathe before being sutured back in place on the patient’s eye (fig 8.4). This procedure of keratomileusis was found by Barraquer to be satisfactory for correction of myopia of even quite severe degree, but was inadequate to correct the high hypermetropia commonly found in aphakic eyes.

In the period before intraocular lens implants were devised there was considerable demand for the surgical correction of aphakia, and Barraquer’s solution was to modify keratomileusis so that, instead of directly shaping the excised lamella of the patient’s cornea, a prelathed donor lamella was sandwiched beneath it to produce the new contour (fig 8.5). This procedure of keratophakia could correct high

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Figure 8.4
Myopic keratomileusis: an excised lamella is shaped on the cryolathe and replaced on the host.

Figure 8.5
Keratophakia: a prelathed lenticule is sandwiched beneath a resected lamella.

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hypermetropia very effectively, and also had the advantage that the donor lenticule could be cryolathed preoperatively rather than while the patient was on the operating table.\(^3\)

In the 1960s and 1970s other surgeons including Troutman and Swinger from the United States of America,\(^4\) and Derek Ainslie from the United Kingdom, started to experiment with the technique.\(^5\) Keratomileusis and keratophakia are, however, extremely exacting techniques requiring specialised equipment and training, and intraoperative complications with the early designs of the microkeratome were not infrequent, with uneven lamellar resection arising from problems such as loss of adhesion of the suction ring, jamming of the microkeratome in the suction ring guide plate, and chatter of the microkeratome blade. Problems also arose during the cryolathing process, such as uneven or eccentric placement of the tissue in the lathe chuck, and variation in the hydration of the tissue leading to variation in thickness of the tissue on freezing. In addition, fluctuation in temperature of the lathe components produced thermally induced dimensional changes. All of these factors, and others, combined to produce unpredictable final refractive results, and for all these reasons the techniques were not widely adopted.

With the introduction of epikeratophakia, ophthalmic surgeons looked forward to a keratorefractive procedure that could not only correct severe degrees of ametropia, but which was simple to carry out and did not require specialised equipment if pre-formed lenticules were obtained from a central manufacturing source.

Surgical technique of epikeratophakia

Before considering the indications for epikeratophakia, it will be helpful to have a basic understanding of the surgical technique involved. It is important from the outset to appreciate that the surgical technique of epikeratophakia for keratoconus is radically different from that for epikeratophakia to correct hypermetropia and myopia. In keratoconus the aim is to compress the ectatic cone with the lenticule, forcing the recipient cornea to adopt a more normal contour, and the success of the procedure depends chiefly on the operative technique of the surgeon. In hypermetropia or myopia the surgeon must avoid causing direct change to the recipient corneal contour at all costs, because the power of the induced refractive change should reside entirely in the configuration of the lenticule, the back surface of which is conformed to follow the shape of the recipient cornea.
Correction of aphakia and high hypermetropia

Historical development of surgical technique

The first attempts to secure an epikeratophakia graft to the surface of the cornea involved denuding a central area of epithelium and suturing the lenticule directly to the superficial stroma. These attempts were unsuccessful because the edge of the lenticule was unstable and the epithelium often grew into the graft-host interface. Significant epithelial ingrowth causes graft failure because the overlying area of the lenticule will not become re-epithelialised causing graft oedema, infiltration with inflammatory cells, and, finally, tissue melting or secondary infection.

To overcome these problems it was necessary to adopt a more invasive approach in attaching the edge of the lenticule to the underlying superficial stroma. The first successfully employed technique used a partial thickness trephine cut with a wedge resection of superficial stroma to create a circular gutter or bed into which the edge of the lenticule was sutured. Thus the edge of the lenticule abutted a vertical edge of peripheral recipient stroma, and it was necessary either to raise the stroma to produce a smooth continuous surface over which the epithelium could migrate or to resect a bed into which the thickness of the peripheral edge of the lenticule could be buried (fig 8.6a). It was, however, soon appreciated that the lenticule requires a greater diameter than that of the trephined bed when it is draped over the central host cornea; it has to reach down into the resected bed to abut with the trephined recipient stroma. The ideal degree of graft-bed diameter disparity was, however, difficult to decide upon, and changes in these parameters were said to lead to improvement in accuracy of refractive results.

Following further research there was a gradual move towards burying the outer edge of the lenticule in a peripherally dissected pocket rather than directly abutting it edge to edge with the host (fig 8.6b). This modification required a still greater graft-bed diameter disparity, and led to an improved margin of safety against epithelial invasion of the graft-host interface. In addition, it removed the graft-bed diameter disparity from being a significant determinant of final corneal contour, allowing this contour to be determined primarily by the lenticule design, together with the tension under which the lenticule was sutured and healed as a secondary main factor. Ultimately, however, the lenticule design and operative technique are interdependent and the specific operative technique adopted will, to some extent, need to be modified with different lenticule designs.
Figure 8.6a
A triangular wedge of superficial stroma excised from the inner aspect of the vertical trephine cut produces a groove in which the edge of the donor lenticule can abut the host stroma.

Figure 8.6b
In the technique without keratectomy, the vertical trephine cut is extended peripherally to form a pocket into which the wing zone of the lenticule is tucked.

Current operative technique

Although this is not a textbook of operative technique, the following overview will allow a good appreciation of the intricacies of undertaking epikeratophakia. With an operating time of 30–60 minutes, either local or general anaesthesia may be employed according to the preference of patient, surgeon, and anaesthetist.
INTRODUCTION TO EPIKERATOFLAKIA

Even if the globe is well exposed and resting in the primary position, superior and inferior rectus sutures are helpful to stabilise the eye and, if there is any ocular deviation, can be used to position the visual axis coaxially with the operating microscope.

A single use disposable trephine blade of diameter 7.5 mm is placed on the recipient cornea, aligned along the visual axis, and a shallow trephination is made by manual back and forth rotation of the blade through less than 90° for two or three turns. The cut should really only penetrate the epithelium and Bowman’s layer, and it is better to err on the side of too shallow a cut rather than too deep. The depth of the cut can be inspected by opening the wound with pressure on the cornea on the inner side of the cut. If the cut is too shallow it can be deepened with a diamond knife, using the depth of the sharpened facet of the blade as a guide to the depth of the incision, aiming for a depth of 0.1-0.2 mm.

The central epithelium is then stripped away, using a blunt curved lamellar blade. Starting centrally, the epithelium is teased off peripherally as far as the trephine cut. The centrifugal motion avoids ruffling up the cut edge of the stroma, which tends to occur if the epithelial removal is attempted centripetally. Epithelial stripping is best carried out in a dry field as this enables one to distinguish any residual epithelial islands clearly.

Ensuring that no residual corneal epithelial cells adhere to the lamellar blade a peripheral lamellar split is created to tuck in the wing zone of the lenticule. By keeping the blade at a flat angle to the slope of the cornea, the split can be made naturally in a single superficial plane, extended outwards about 1.5 mm.

The lyophilised lenticule which will have been rehydrating for 5 or 10 minutes is then applied and the first cardinal suture of 11/0 Ethilon placed about 1.5 mm from the edge of the lenticule, with the needle emerging through the split edge of the tissue. Once the first four cardinal sutures are in place a check is made on the centration of the lenticule and, if necessary, any sutures with incorrect tension replaced. Only at this point is an attempt made to tuck the wing zone of the lenticule into the peripheral lamellar split. A further four sutures are placed into the oblique meridians and this is generally enough to give adequate stabilisation of the lenticule (fig 8.7).

After administration of a subconjunctival antibiotic and steroid injection a temporary tarsorrhaphy suture is placed. A 6/0 Mersilene suture is passed through the grey line in the midline of the palpebral aperture with the second bite made more temporally. This leaves sufficient lid laxity medially to allow daily examination of the state of re-epithelialisation of the graft.

Overzealous tensioning of the sutures will lead to flattening of the underlying host cornea and reduction of the steepening effect of
a hypermetropic lenticule. For this reason the minimum surgical intervention compatible with stabilisation of the lenticule on the recipient is required. Once a lenticule has an intact and watertight epithelial covering, the compacting forces induced by the endothelial
Figure 8.7c
Débriding the epithelium centrally.

Figure 8.7d
Aspiration of débrided epithelium.
Figure 8.7e
Dissection of the peripheral lamellar pocket.

Figure 8.7f
Irrigation of lamellar pocket to remove any loose epithelial cells.
pump function deturgescing the donor and host tissue will give the graft reasonable stability even before there is significant wound healing at the graft-host junction. Thus the method of surgical fixation need only be effective for a fairly short period of time. By using a suture material with minimal breaking strength the tendency to exert
too much traction on the graft is reduced. If the graft appears to be satisfactorily stabilised with the first four cardinal sutures, then fixation is likely to be adequate.

Studies have been made to find alternative modes of graft fixation which could be simpler, quicker, or less prone to surgical error. Fibrinogen based adhesive has been shown to be both quick and effective in bonding refractive epikeratophakia lenticules. 6,7 Com-

**Figure 8.7i**
With eight sutures in place, the wing zone can be tucked into the lamellar pocket.

**Figure 8.7j**
Burying the 11/0 nylon suture knots.
commercially produced adhesive (for example, Tisseel) is widely used in many areas of surgery but does not have a drug licence in the United Kingdom as a result of the concern over possible viral disease transmission, because the material is derived from pooled plasma from multiple donors. Fibrinogen can be derived from individual patients by cryoprecipitation and used successfully as a biological adhesive to glue epikeratophakia lenticules. As the process is, however, time consuming on an individual basis, surgeons will probably await the availability of a good biologically compatible biosynthetic adhesive for gluing their epikeratophakia grafts. It is of course possible to perform epikeratophakia without adhesives or sutures, but the risk of graft loss or wound dehiscence would seem to merit the little time and effort required in suturing.

Most grafts will re-epithelialise satisfactorily irrespective of the postsurgical management regimen. In those cases where there is delay in the establishment of primary epithelial cover, however, severe problems may arise and the patient’s management may often be difficult. A temporary tarsorrhaphy suture is well tolerated in most cases and almost certainly expedites primary re-epithelialisation, and thus should probably be carried out in most patients. It is not of course a panacea, and a bandage contact lens is a good alternative for some patients, for example, when it is the only seeing eye that is being operated on. Special steep bicurved lenses can be used, particularly in infants, but many patients can be fitted with a standard bandage lens (Plano Permalens BCOR 8.0, Bausch & Lomb). Whatever type of bandage lens is used, close postoperative monitoring is required, because in a small proportion of cases the lens will become “sucked on” and cause inflammation.

Where the surgery is carried out under local anaesthesia, it may be difficult to place a temporary tarsorrhaphy suture without extra anaesthetic blocks to the eyelid. An alternative in this situation would be to use cyanoacrylate adhesive as a temporary tarsorrhaphy.

A tarsorrhaphy suture is unsuitable in children, and also in the mentally handicapped or mentally disturbed. In these patients, examination of the eye through a partially closed eyelid is generally impossible, and removal of the tarsorrhaphy suture would probably require further anaesthesia. In these cases a temporary ptosis induced by botulinum toxin A at the time of surgery offers a good alternative; 0.1 ml of botulinum toxin (equivalent to 20 units) is injected through a one inch 20 gauge needle into the levator palpebrae superioris, and will usually give complete ptosis by the first or second postoperative day. In those patients where the application of postoperative topical eye treatment is likely to be difficult, a sub-Tenon’s depot steroid can be given but this is best avoided, except in extreme cases, because of the risk of secondary glaucoma or the potentiation of infection.
When there is pre-existing idiopathic or iatrogenically induced astigmatism, simultaneous relaxing incisions can be made into the epikeratophakia bed to correct the astigmatism beneath a spherical powered lenticule.\textsuperscript{14}

**Correction of keratoconus**

The surgical technique of epikeratophakia for keratoconus bears little relation to that used for the correction of aphakia. The initial stages of trephination and epithelial stripping are similar, but the application of the lenticule requires multiple sutures secured with sufficient tension to compress and flatten the underlying cone. The early protocols for the procedure recommended compression of the lenticule with a graft spatula by the assistant to help achieve sufficient tension in the sutures. Even paracentesis of the donor anterior chamber was attempted in order to soften the eye and achieve adequate compression. Such manoeuvres are not, however, necessary if one accepts that the compression of the underlying cone is achieved only gradually during the operation, the initial sutures becoming slack as tension in the lenticule is built up, and that a number of the early sutures will need to be replaced before a uniform tension is developed in the graft.

Given that 16, or more usually 24, interrupted sutures of even tension are required, it becomes apparent that the procedure inevitably takes 1.5–2 hours to complete. As the typical patient will be a young or middle aged adult, general anaesthesia is usually preferred by both patient and surgeon. Unfortunately, with the common association of keratoconus with asthma, and in Down’s syndrome with cardiac defects, the choice of general anaesthesia does not necessarily offer a relaxing occasion for the anaesthetist.

With younger patients it must be remembered that the globe is more readily subject to distortion, and that the rectus stay sutures should not be overly tensioned, especially during the trephination. A typical procedure will involve a 7.5 mm trephine cut centred over the cone. The standard size lenticule used for keratoconus is 9 mm in diameter, plano powered, with a nominal thickness of 0.3 mm, and a small tapering wing zone. Preparation of the graft bed proceeds as for an aphakic epikeratophakia graft. Suture strength should be sufficient to induce considerable tension in the graft material and 11/0 Mersilene is not only strong but also non-biodegradable, and can thus be left in situ indefinitely. This may be a considerable advantage if the final topographic contour is satisfactory and actively maintained by suture tension.
After the first eight sutures are placed, the graft wing can be tucked into the bed and a check on the sphericity of the graft surface made with a qualitative handheld keratometer. When reasonable sphericity is achieved by selective suture replacement, then a further 16 sutures may be placed, situated in pairs in the remaining gaps. At conclusion the suture knots are buried and a final check of the graft contour made with the keratometer.

In view of the prolonged operating time there is a risk of retinal phototoxicity from the operating microscope, so a 4 mm diameter light shield should be employed after the first four cardinal sutures have been placed.

If there is significant corneal scarring in association with the patient’s keratoconus, this will limit the degree of visual recovery, but does not necessarily preclude epikeratophakia as the surgical procedure of choice in certain patients. Minor degrees of superficial scarring, such as a small isolated proud nebula, can be resected surgically at the time of stripping the epithelium, or by prior photoablation with the excimer laser, but the visual prognosis must inevitably be guarded in such cases.

A mild degree of eccentricity of the cone is easily compensated for by intentionally decentring the placement of the trephine cut and position of the lenticule, and preoperative topographic analysis of the cornea is most useful in planning this aspect of the operation. Where the cone is particularly eccentric, and if corneal thinning extends right up to the limbus, then a larger lenticule should be used.

As a result of the frequent association of Down’s syndrome with cataract and keratoconus, it is not uncommon to find that such patients present with both a mature cataract and an advanced cone. It is also not uncommon for these patients to have atopy, chronic allergic conjunctivitis, and a tendency to eye rubbing, making them a poor risk for penetrating keratoplasty. It is reasonable in this situation to proceed with simultaneous combined lens aspiration, intraocular lens implantation, and epikeratophakia for keratoconus.

In anticipation of both poor compliance with treatment postoperatively and eye rubbing in such patients, small incision cataract surgery with a folding silicone lens implant is certainly to be preferred. Eye rubbing or banging may have produced some degree of zonular dehiscence, but fortunately the lens is unlikely to be sclerotic and can usually be aspirated without the use of phacoemulsification. It is important to complete the trephination and epithelial stripping before the eye is opened and, in view of the poor corneal rigidity in keratoconus, it is also advisable to form the peripheral stromal pocket, in spite of the fact that this will give some impairment of the operating view during the cataract extraction.
Finally, sub-Tenon's depot steroid will reduce the need for postoperative topical medication, and a ptosis induced by botulinum toxin will help promote re-epithelialisation. Where there is pre-existing aphakia and keratoconus it is possible to attempt to correct the aphakic refractive error at the time of epikeratoplasty by the use of a positive powered lenticule, but obviously the final keratometry of the host cornea beneath the lenticule can only be guessed at preoperatively. A satisfactory refractive outcome from such a procedure is, however, reported.18

Manufacture of epikeratophakia lenticules

Most epikeratophakia procedures carried out worldwide have used lenticules prepared by American Medical Optics/Allergan during the period 1984–92. Exact details of their tissue processing and preparation techniques have not been published, but all the corneas were cut by cryolathing and most were freeze dried before dispatch. For a surgeon wishing to carry out epikeratophakia, precut lenticules are available from a number of manufacturing centres, including Keratec Eye Bank (St George's Hospital Medical School, London) and Bristol Eye Bank (Bristol Eye Hospital).

Alternatively, surgeons may wish to prepare their own lenticules in which case there is currently quite a wide range of techniques and equipment available to achieve this. All techniques have in common the need for donor corneal tissue from which to manufacture the lenticule, and the selection of donor tissue is an important consideration.

Selection of donor tissue

In North America and Europe there is currently no absolute shortage of corneal donor tissue because there are many potential cadaveric donors, and the supply and demand for corneal tissue are dictated primarily by the financial constraints of the costs of running the eye banks. For eye banks to supply sufficient tissue of consistent quality for penetrating keratoplasty, there are inevitably surplus corneas which, although satisfactory by other criteria such as microbiological screening, are unsatisfactory because of poor endothelial cell count. By using only such corneas for epikeratophakia surgery, the proportion of donor corneal tissue that is actually transplanted is maximised and
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there are thus ethical and financial arguments to support such an arrangement.

This is not to say that the quality of tissue used for epikeratophakia surgery is not just as important as in penetrating keratoplasty, and indeed it is likely that many factors such as donor age, keratometry, corneal diameter, corneal thickness, and corneal hydration influence the outcome of an epikeratophakia procedure. Most tissue held in European eye banks is stored in organ culture at 34°C, and corneas preserved in this way undergo considerable stromal swelling. Control of the thickness of the cornea when cutting a lenticule is of fundamental importance and various approaches to this problem have been made. In vivo, there are natural anatomical variations, as well as small physiological diurnal fluctuations of corneal thickness and hydration, and there is thus no single normal measurement for either variable, although their variations are inevitably interlinked. There are much wider fluctuations of these parameters post mortem, and in conditions of corneal storage, with corneas often twice physiological thickness, some form of control is mandatory when processing tissue into lenticules.

Safir and co-workers devised a corneal press in 1983." This compresses an oedematous cornea between two sintered glass conformers to produce a corneal button of standard thickness, but not necessarily of standard hydration. An alternative approach proposed by Barratt is to control hydration by osmotic means. Either method of rendering the cornea into a more physiological state can be applicable to the preparation of lenticules in the wet state. For preparation of lenticules by cryolathing, however, the freezing increment caused by the expansion of the tissue from ice formation needs to be taken into consideration and, therefore, the primary control of hydrational state might be considered preferable to thickness control, although there are no published data of comparison of these two methods.

Cryolathing

Cryolathes are available commercially from Steinway Instrument Company (California, USA) and from CityCrown (Aylesbury, Bucks, UK).

Tissue to be cryolathed is generally dyed with a vital dye such as Kiton green. This enables the tissue to be clearly distinguished from any ice that will tend to form on it and on the lathe chuck from condensation of atmospheric moisture. In the conventional method
of tissue cutting the corneal button is placed on a cutting base of standard curvature.

Once the cornea is frozen the corneal thickness should be measured, because the freezing increment in thickness is unpredictable. Unfortunately, at this stage conflicting demands are placed on the cryolathe operator. As the chuck and cutting tool are cooled there will be thermally induced dimensional changes in the lathe. The effect of these can be minimised by two strategies—either proceeding with the lathing according to a swift and strict timetable under which it is assumed that any dimensional changes are standardised and can thus be compensated for, or allowing the temperature of the lathe to reach a steady state. This then enables the lathing to proceed at an arbitrary pace, but has the disadvantage of progressive ice build up which can obscure the tissue.

To prevent the thermally induced dimensional changes in the lathe affecting the measurements on the lathe headstock verniers, the positioning of the cutting tool in relation to the tissue base is established initially as a zero point, and measurement of tissue thickness can then be directly related to this reading. From the measured corneal thickness, the lathing parameters may then be calculated and the cutting started.

On a machine with a single radius cutting arm, it will be necessary to cut the optic zone and the wing zone as two separate procedures. On a lathe with a dual radius cutting arm, both the optic and wing zone parameters can be set simultaneously, and the lenticule cut in a single manoeuvre. Cryolathing produces an excellent quality of finish to the cut surface with the minimum of operator experience. The procedure is technically exacting, and requires a close attention to detail, an understanding of the potential sources of error in setting up and maintaining the lathe, and an ability to correct them.

An alternative method of cryolathing devised by Barratt employs a variety of precarved chucks of complex configuration, which simulate the desired final configurations of the anterior epi-keratophakia lenticule surface. The tissue is conformed on to the chuck and the back surface is then cut with a single curve of radius equal to that of the average recipient keratometry. There are no directly comparable data available at present to compare this method with the conventional cutting techniques.

The advantages of cryolathing are that it produces the best quality of cut finish, that rotary lathing systems are an excellent method of cutting spherical surfaces, and that there is a good body of knowledge regarding the technique. Its chief disadvantages are that there is an uncontrolled freezing increment in the thickness of the corneal tissue, and that it is necessary to make compensational adjustments for this and the thermally induced changes in the lathe. It has also been
argued that freezing the tissue damages it and causes erratic refractive results, tissue haze, and epithelial instability, but there is little evidence to substantiate these assertions.

**Microtome cutting**

This technique, described by Hjortdal and Ehlers, uses a histological microtome to cut the frozen corneal tissue. As only plano cuts can be made with such an instrument it is necessary for the tissue to be conformed on to a preshaped brass base, and then cut. The cutting of a bicurved lenticule to correct myopia is achieved by sequential conformation and cutting, first on a concave base and subsequently on a convex one. Results of correction of high myopia using lenticules manufactured by this technique have been reported.

**Lathing at room temperature/dry state lathing**

An alternative to lathing in the frozen state is to lathe the cornea in a semi-desiccated state. This can be carried out on a standard contact lens manufacturing lathe. The technique was devised by Maguen et al., who lyophilised corneas and then made the dried tissue adherent to PMMA bases using a concentrated sucrose solution in a two stage process. The technique was modified by Rostron et al. to simple partial desiccation of the cornea before lathing. The corneal button is first soaked in a dextran and dextrose solution, and placed on a standard curved PMMA base. After drying over silica gel for 48 hours at 4°C the cornea becomes adherent to the base as a result of the viscosity of the dextran and dextrose. In its semi-dry state the cornea can be cut with a diamond tool at ambient temperature, so avoiding the thermal and freezing induced dimensional changes encountered on the cryolathe. The tissue is cut in a relatively compacted state compared with the relatively expanded state encountered with cryolathing, making the accuracy of measurements of the tissue more stringent. There are no direct comparative trials of dry state versus cryolathing.

**Wet state preparation**

There are a number of systems available for cutting epikeratophakia lenticules from tissue in the wet state using a motorised
microkeratome. As the microkeratome can make only a flat cut, to create lenticules with refractive power it is necessary to deform the donor cornea over a preshaped mould, such that the endothelial side of the tissue can be cut in a flat plane with the microkeratome.

The BKS 1000 (Barraquer–Krumëich–Swinger 1000 System, Eyetech-MVA Ag, Balzers, Liechtenstein) has the longest track record. This uses a Barraquer style microkeratome with an oscillating blade and an artificial anterior chamber for mounting a corneoscleral segment. Plano lamellae can be resected from the donor tissue by driving the microkeratome across the corneal surface guided along dovetails coated with Teflon in the refractive bench. The thickness of the resected lamella is controlled by a thickness plate inserted into the front of the microkeratome. Such plano powered lamellae can be used as lenticules in epikeratophakia for keratoconus.

To produce powered lenticules the tissue is placed epithelial surface downwards on a preformed plastic mould, and held in place by vacuum exerted through small perforations in the mould surface, as well as by a serrated stabilisation ring in the periphery. Again the tissue is cut by running the microkeratome across the back surface.

Under the scanning electron microscope, the cut surface of the tissue can be seen to be considerably rougher than the cut surface obtained with the cryolathe. This is not surprising because the oscillating microkeratome blade comes to rest at the end of each excursion, and the tissue in the wet state can be more readily pulled and torn than when it is frozen. It is, however, debatable whether the quality of the cut has any bearing on the clinical outcome, because even handcut plano lenticules have been used successfully clinically.

A more recently developed microkeratome system devised by Buratto uses a similar principle to cut refractive lenticules. In this system the microkeratome head is on a flexible drive shaft which, it is claimed, reduces the chances of the cutting head jamming in the guide plate and producing an irregular cut.

Another microkeratome system has been developed by Draeger et al. and has a continuously rotating circular blade rather than an oscillating one. This blade has a continuous cutting motion and the quality of cut surface is said to be better than that obtained with the other microkeratome systems. Comparative clinical evaluation of the various systems has not, however, been made.

The claimed advantage of wet state preparation is that there is less tissue damage and that this is reflected in a more rapid visual rehabilitation with a reduced incidence of complications such as epithelial instability. Again, little in the way of prospective comparative trials has been carried out although there is a report.
that the refractive accuracy of the BKS 1000 system was similar to that obtained with cryolathed lenticules manufactured by Allergan.

Excimer laser cutting

Baumgartner et al have described an experimental method of cutting lenticules with an excimer laser. The tissue is moved in three dimensions by a computer controlled system to expose different areas of the tissue to the photoablative laser beam. There still have to be reports of clinical cases using such a system.

Postoperative management

Initial postoperative treatment in the compliant patient is usually a topical mydriatic and antibiotic drops, for example, gentamicin 0.5% and cyclopentolate 1%, both three times a day. Where there is poor compliance, as in young children and the mentally handicapped, an oral systemic antibiotic such as amoxycillin paediatric elixir 250 mg three times a day may be substituted.

Until epithelial cover is established over the graft there is increased risk of graft infection, and it seems prudent to avoid topical steroids until this time. There are, however, exceptions to this: firstly, in patients who have had previous uveitis the surgical trauma may well reactivate the inflammation and they are likely to need steroid cover from the start, in proportion to the anticipated severity of reaction. Another exception is when there is a progressive, reactive, postsurgical inflammation which reaches a point where its severity is sufficient to inhibit graft re-epithelialisation. When this occurs a vicious circle is created because the persistence of an epithelial defect on the graft in itself perpetuates the inflammatory reaction. This phenomenon can sometimes be observed in simple traumatic corneal epithelial abrasion, and as such is not peculiar to epikeratophakia. It does, however, underline the necessity for very close observation of the patient in the early postoperative period. Although it is not necessary for patients to remain in hospital, daily follow up and documentation of the state of epithelial cover should be carried out until the graft is fully re-epithelialised. This is usually between the third and fifth postoperative day and, once an intact epithelial cover has been established, the temporary tarsorrhaphy suture can be removed and topical steroids started.
At this point treatment can typically be changed to cyclopentolate 0.5% drops and betamethasone with neomycin ointment, both three times a day, with an ointment based application preferred to protect and stabilise the epithelium. The epithelium at this stage is tenuous and there will often be a vortex keratopathy and marked punctate epithelial staining with fluorescein. Punctate staining may persist for some months, and specular micrographic observation of the epithelium can show abnormalities persisting even one year postoperatively. Measurement of the physiological barrier function of the epithelium demonstrates that this returns to normal around two months after surgery.

Although the establishment of primary epithelial cover is a major step forward in the postoperative progress, continued close observation is necessary to avoid secondary epithelial breakdown, which is most likely to occur in the early weeks before the epithelium has had a chance to stabilise. The problem is particularly likely to arise if any of the corneal sutures become loose, because these will attract mucus and polymorphonuclear leucocytes, and will create a local inflammatory nidus. If allowed to persist, this inflammation is likely to produce local secondary epithelial breakdown, as well as stimulating peripheral neovascularisation. Thus any suture that appears loose should be removed immediately, and patients instructed to return between scheduled postoperative visits if they experience persistent foreign body sensation in the eye.

If a secondary epithelial breakdown occurs, apart from the removal of any loose sutures, the eye should be treated by continuous padding, a bandage contact lens, or a botulinum toxin induced ptosis until the epithelial cover is re-established and the epithelium stabilised. Any eye drops that are required should be preservative free if a bandage lens is worn.

In refractive epikeratophakia for hypermetropia or myopia, the sutures are necessary only to stabilise the lenticule until an intact epithelial cover is established. They can thus be removed at any time after this has occurred, and are typically taken out at one or two weeks postoperatively.

In keratoconus the situation is very different, because it is necessary for there to be adequate stromal wound healing before the sutures can come out. Fortunately, topical steroid application can be kept to a minimum and can usually be discontinued after a couple of months. As well as the dose and duration of steroid application, the patient's age is an important factor in the estimation of time required for adequate wound healing. In a teenager there will probably be adequate wound strength by two months, but in adults 3–4 months should elapse before considering elective suture removal. This should then be guided by the corneal topography, because there is likely to
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be an element of suture induced astigmatism and, if so, selective suture removal with a further pause for stabilisation of the topography should be considered.

Complications

Epithelial breakdown

The most common cause of epikeratophakia graft failure is stromal melting or scarring associated with defective epithelial cover. Thus management of epikeratophakia graft patients revolves around prophylactic measures to attain swift primary graft epithelialisation and close attention to care in the early few postoperative weeks to avoid secondary epithelial breakdown.

If secondary epithelial breakdown does occur, the rate at which the epithelial defect heals will be found to be considerably slower than the rate at which grafts undergo their normal primary re-epithelialisation. Any area of stroma that lacks epithelial cover will become infiltrated with inflammatory cells, and with time these will destroy the normal tissue architecture and make re-epithelialisation more difficult. Sometimes it can be seen that a barrier of slightly swollen epithelial cells is apparent at the border of an epithelial defect, and these can inhibit any tendency for their neighbouring cells to migrate. If the epithelial border is grasped with fine forceps a string of epithelial cells can be pulled away, leaving a ragged edge of adjacent epithelium. This new epithelial border is no longer inhibited from migration, and so this manoeuvre can stimulate rapid epithelial cover of a defect that has been static in size for some days.

It will, however, be found that any defect that persists for more than a week or two is likely to leave some subepithelial scarring and local topographic irregularity. If this prejudices the final visual outcome, then the area can be treated by phototherapeutic keratectomy, but it is best to leave the eye for a good many months before judging whether further intervention is justified. On the other hand, if there is a major degree of stromal melting, it may be better to proceed directly to epikeratophakia graft exchange.

Infection

Infection is obviously a very serious but rare complication of epikeratophakia and will generally be seen arising in the first few
postoperative days, or at a later stage in association with suture loosening or a secondary epithelial defect.\textsuperscript{33} After taking culture swabs and a Gram stain from the infected area and starting topical antibiotics, the patient should be followed very closely. If there is no significant improvement within 24 hours the graft should be removed because it is not worth risking the infection becoming established in the host cornea.

**Interface opacities**

If sufficient care has not been exercised in the operating room, on slitlamp examination microparticulate debris may be seen trapped between the host Bowman's layer and the graft.\textsuperscript{34} Any epithelial cells left in this plane undergo proliferation and form a grey–white blob-like opacity. If this is localised away from the visual axis, it may well not affect the visual outcome. A more extensive epithelial proliferation may lead to an opacity which extends into the visual axis. This can be treated surgically by opening up the wound in one quadrant and mechanically débriding the cells from the interface.\textsuperscript{35} One should, however, observe the natural course of an epithelial island for a month or two before resorting to corrective surgery, because a proportion of epithelial islands will undergo spontaneous involution. The occurrence of interface haematoma from bleeding of pre-existing corneal new vessels has also been described and can be managed surgically in a similar fashion.\textsuperscript{36}

**Residual ametropia**

Visual recovery and stabilisation of graft topography are slow and, although a good estimate of a final probable outcome can be made at six months postoperatively, there will be further refractive and keratometric change over the ensuing six months, so that it is inadvisable to consider surgery for further minor refractive adjustment until one year postoperatively. Residual degrees of astigmatism can be treated by selective suture removal or, if this option has been exhausted, by further tension suture placement in conjunction with relaxing incisions made at the graft–host junction in the steep meridian.\textsuperscript{37}

In myopic epikeratophakia, general excess suture tension seems to steepen the central cornea, giving undercorrection, with suture removal increasing the degree of correction obtained.\textsuperscript{38} Once all
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sutures are removed, undercorrection of spherical errors may result from excessive tension in the wound and can be reduced by circular trephination at the graft-host junction to relax the incision throughout the 360°. Alternatively, residual refractive error can be tackled by photorefractive keratectomy of the epikeratophakia lenticule. In myopia this has been reported to be complicated by scarring of the lenticule, but successful reduction of overcorrection without scarring in a hyperopic lenticule is documented. Radial keratotomy in an intact epikeratophakia graft has also been described.

Physiology and histopathology

Most studies of epikeratophakia have been made on grafts with cryolathed lyophilised lenticules. In the preparation of a lenticule by cryolathing, the epithelium is removed by mechanical stripping, and the endothelium and Descemet's membrane removed by the lathing process. Thus the only cells remaining in the lenticule are the keratocytes in their surrounding collagen matrix. Although it is possible to achieve keratocyte survival following cryolathing by the use of cryoprotectant solution, this is not generally employed and is irrelevant if the tissue is subsequently to be freeze dried, because the keratocytes will not survive the lyophilisation process. The advantage of lyophilisation is that it allows the lenticules to be stored at room temperature with a nominal shelf life of several months. A comparative trial of storing lenticules in a lyophilised or wet state was carried out by Allergan in 1987, and no advantage was found in the wet state preservation system, which was considered to give a shorter shelf life.

When transplanted, the keratocytes in the donor stroma break up and the cellular debris is quite rapidly dispersed, so that within 24 hours postoperatively the donor stroma will appear amorphous and devoid of cells. Epithelialisation of the lenticule can be observed clinically to give graft cover within a matter of days, but the establishment of an epithelial cell layer that looks normal on slitlamp examination can take some months. In spite of a normal clinical appearance, on specular microscopy such an epithelium can be shown to be deficient in cellular thickness and maturity. Re-innervation of epikeratophakia lenticules appears to be largely absent, so trophic changes in the epithelium are only to be expected. The migration of keratocytes into the lenticule proceeds at a much slower pace, with the cells gradually migrating in from the graft periphery. Overall keratocyte density may still be low several years after grafting. The lack of keratocytes in the graft stroma does not appear to cause any
problem, and if one is to conjecture that the pathological process responsible for keratoconus is abnormal maintenance of the structural stromal matrix resulting from disorganised keratocyte activity, then in epikeratophakia for keratoconus the longer the delay before the host keratocytes start to degrade the lenticule stromal matrix the better. During the 15 years that epikeratophakia has been carried out there has not been a clearly documented case of recurrence of keratoconus in a patient having epikeratophakia. There have also not been any documented cases of rejection of epikeratophakia grafts.

Pepose et al showed that the HLA (human leucocyte antibody) class I antigens are present on the donor keratocytes in lyophilised lenticules, but postulated that the tissue's lack of immunogenicity was the result of the short time that the recipient was exposed to the donor antigen, and the lack of augmentation of antigenic expression that is thought to occur in graft rejection.\textsuperscript{48, 49} Other workers have conducted elegant experiments on the fate of lyophilised grafts. Moore et al carried out xenografts between cats and rabbits and found that, even in systemically presensitised recipients, there was no evidence of rejection of interlamellar intrastral lyophilised xenografts.\textsuperscript{50} In a second experiment to maximise the potential for rejection, xenogeneic penetrating keratoctoplasties were carried out in eyes that had previously undergone successful xenogeneic lyophilised intrstral implants. Although rejection with marked vasularisation and graft opacification was observed in the penetrating grafts, the immediately adjacent lyophilised graft tissue did not become involved in the rejection process. This lack of response implies that patients receiving lyophilised tissue are not exposed to an enhanced risk of rejection should they require penetrating keratoplasty at a later date.

Further work by Frantz et al compared the lyophilised epikeratophakia homografts in rabbits with fresh tissue epikeratophakia homografts prepared with the BKS 1000.\textsuperscript{51} The grafts were implanted on to systemically presensitised recipients and also on to presensitised recipients with prevascularised corneas. In no cases were the lyophilised epikeratophakia grafts rejected, but the fresh tissue grafts prepared by the BKS 1000 were rejected in the presensitised, prevascularised recipients.

**Indications for epikeratophakia**

**Keratoconus**

For an ophthalmologist managing a patient with keratoconus, decision making with regard to surgical intervention has never before been
so easy or so difficult. Epikeratophakia for keratoconus now offers a safe and reversible surgical option in comparison to the more risky and irreversible procedure of penetrating keratoplasty. The risks and benefits of either procedure are quite distinct, so it would be nice to think that their respective indications were clearly defined but these are, however, not well established. The situation is indeed further complicated by the choice of the third surgical option of lamellar keratoplasty, or by the pursuit of a line of medical management with contact lenses. There are thus two questions for the patient and ophthalmologist to answer—should surgery be undertaken and, if so, which procedure should be carried out. Epikeratophakia is but one of the major therapeutic advances that have been made over the past 30 years in the management of keratoconus, and inevitably the pattern of these historical developments colours attitudes towards current management strategy. The situation is made all the more difficult with keratoconus being a chronic condition of unknown aetiology and uncertain prognosis. For these reasons, all that can be said with certainty is that none of our current management strategies has been scientifically evaluated or proved for the long term management of this condition.

Management with contact lenses

The diagnosis of keratoconus generally comes to light when best corrected acuity (BCVA) with spectacles is found to be reduced. The introduction of contact lenses has been a tremendous boon to this group of patients who hitherto had to reconcile themselves to varying degrees of visual impairment or handicap. The early scleral or haptic contact lenses could be made to fit virtually any degree of severity of cone, but were cumbersome and poorly tolerated, not infrequently inducing scarring and neovascularisation of the cornea. The introduction of corneal microlenses improved lens tolerance, and current designs can be fitted in all but the most ectatic cones. With the options of mixed material lenses such as SoftPerm (Synergicon A, Sola Barnes Hind, Sunnyvale, CA, USA), or piggy back hard on soft lenses, there is virtually no case that cannot obtain visual improvement by the fitting of contact lenses. There is, however, often a disparity between what can be achieved with a trial fitting and the patient’s tolerance and compliance with the prescribed lenses. The not infrequent association of keratoconus with atopy and with mental subnormality will often make contact lens wear difficult or impossible. Even with good compliance and acuity, the long term wear of contact lenses may be associated with apical subepithelial scarring with reduction of acuity, and the possibility of the eventual need for
penetrating or lamellar keratoplasty rather than a less invasive epikeratophakia procedure. Progression of keratoconus may continue beneath a contact lens to the point of acute hydrops. This will generally result in the need for penetrating keratoplasty, whereas an earlier decision to intervene surgically would have given a wider range of effective surgical options.

Management by penetrating keratoplasty

Historically, penetrating keratoplasty has been the only alternative option to contact lens wear for keratoconus patients. Undoubtedly, the results from penetrating keratoplasty can be excellent, and have improved over the years with the introduction of microsurgical techniques, viscoelastics, improved suture materials, eye bank storage, and tissue evaluation methods. A study by Epstein et al in 1987 of 345 patients undergoing penetrating keratoplasty for keratoconus showed 92% graft survival at three years excluding primary graft failures. It must, however, be remembered that graft survival curves show continuous attrition over the years as a result of endothelial failure and graft rejection. In addition, graft survival is not synonymous with visual restoration because, quite apart from the not infrequent astigmatism, due account must be taken for associated morbidity from steroid induced cataract formation and secondary glaucoma. In Epstein’s study the prognosis for regrafts deteriorated rapidly at each repetition of surgery, with three year survival for a second graft being 86% and for a third graft 50%. A successful penetrating keratoplasty with minimal astigmatism and prolonged graft survival offers as good a “cure” for an otherwise intractable condition and yet, when things go wrong, the patient’s problems are often compounded. It is thus not surprising that surgical intervention in keratoconus has been considered an option of last resort to be entertained only after the eye has developed acute hydrops, or where there is complete failure to tolerate contact lenses.

Management by lamellar keratoplasty

Lamellar keratoplasty has enjoyed a variable popularity in the management of keratoconus. Its freedom from failure caused by rejection has given it some favour in spite of its difficult surgical technique. In comparison to the excellent visual results generally obtained with a penetrating graft, however, acuity following lamellar grafting is often less than patient or surgeon would wish, and so lamellar grafting has never been widely popular. Recent advances
such as the use of air dissection to achieve deep lamellar resection have given a new impetus to this surgical approach.\textsuperscript{53}

Lamellar keratoplasty probably carries a risk of complications and morbidity intermediate between that of epikeratophakia and that of penetrating keratoplasty. It is likely to achieve a better visual result than epikeratophakia when there is significant corneal scarring or marked variation in central corneal thickness.

\textit{Management by epikeratophakia}

Results of epikeratophakia for keratoconus were first published in 1982 by Kaufman and Werblin and co-workers from Louisiana State University.\textsuperscript{54, 55} Soon afterwards a nationwide study of epikeratophakia was started by Allergan with 200 grafts having been performed by 1986. Analysis of the first 82 cases was published at that time, showing improvement of unaided visual acuity in all but two cases, with a considerable improvement of BCVA in most patients. The initial protocol for entry into the study required an acuity of 6/12 or better with a diagnostic "hard" contact lens and that any corneal scars should be at least 1 mm from the visual axis. It had originally been intended that some patients such as those with Down's syndrome and central corneal scarring should be excluded from the data analysis, but in fact the results in these patients proved so encouraging that most were incorporated into the published series.

Subsequently, a number of comparative trials have been carried out where patients have been randomly allocated to penetrating keratoplasty or epikeratophakia surgery. McDonald \textit{et al} studied 36 eyes at an average follow up time of 21 months and found no significant difference in BCVAs.\textsuperscript{56} Selection criteria included a preoperative BCVA of 6/12 or better. Postoperative graft rejection was seen in eight of the 17 eyes with penetrating keratoplasty, but none of the grafts was lost during this follow up period. A similar study by Steinert and Waggoner on 20 patients followed for a mean of 25 months came to similar conclusion.\textsuperscript{57} They observed that time to visual stabilisation was more rapid in penetrating keratoplasty (about three months) compared with epikeratophakia (about one year).

A larger comparative trial of two groups of 30 patients followed for three years was published by Fronterre and Portesani in 1991.\textsuperscript{58} They showed that contrast sensitivity recovered more rapidly in the penetrating keratoplasty group, but that after one year's follow up there was no longer any significant difference between the two groups. In their series the rejection rate in penetrating grafts was 10%, but there were no graft losses. The conclusion from the study was that epikeratophakia provides satisfactory clinical results in
early or intermediate stages of keratoconus, whereas penetrating keratoplasty may be reserved for cases with central scarring and/or high protrusion of the cornea. Another comparative study by Goosey et al showed an equal proportion of patients achieving 6/12 vision following either penetrating keratoplasty or epikeratoplasty (93%), but a higher percentage of 6/6 acuity in the penetrating keratoplasty group (73%) compared with the epikeratoplasty group (24%).

Although in selected patients undergoing either epikeratophakia or penetrating keratoplasty it may not be possible to demonstrate significantly different visual outcomes, the visual effects are undoubtedly different. A patient with “successful” penetrating keratoplasty in one eye and “successful” epikeratophakia in the other will most likely tell you that the vision is better in the eye with the penetrating keratoplasty (fig 8.8). The arguments for doing epikeratophakia rather than penetrating keratoplasty lie in the long term graft survival and reduced morbidity associated with epikeratoplasty. It does, however, mean that particular care needs to be taken in selecting and counselling patients for any particular surgical operation. A patient undergoing epikeratophakia with “unilateral” keratoconus who has never worn a contact lens is likely to be pleased if the vision improves from counting fingers to 6/12. On the other hand, a patient with a similar degree of keratoconus in both eyes might present for surgery as a result of poor contact lens tolerance, but having been used to obtaining 6/6 with contact lenses, is likely to be unhappy with a 6/12 postoperative result, and so his or her surgeon will wisely opt for a penetrating keratoplasty. If this is successful then a compromise visual result in the second eye may be acceptable, in view of the reduced operating risks and probable better long term prognosis for graft survival. Then again, if the penetrating keratoplasty in the first eye should fail, there are different arguments for doing epikeratophakia in the second eye.

Some patients coming to surgery will wish to take the path with least risk and so prefer to have lamellar keratoplasty or epikeratoplasty. If the visual result is poor, they still have the option of proceeding to penetrating keratoplasty at a later date, albeit with a loss of potential seeing time. In this situation the risk of presensitisation of the eye to donor antigens is likely to be of some consequence to the eventual outcome of a penetrating graft. As such, the experimental work in animal models gives a strong argument for the use of freeze dried donor tissue. Whether the use of freeze dried epikeratophakia grafts does prejudice the outcome of a subsequent penetrating keratoplasty in humans may never be proved, as a result of the inevitable small numbers of patients and varied management protocols.

Some data on this subject are available; a report in 1988 by Frantz et al from Louisiana State University documented the progress of
**Figure 8.8a**
Penetrating keratoplasty for keratoconus with clear graft and prominent scarring at graft-host junction.

**Figure 8.8b**
Epikeratophakia for keratoconus in other eye of same patient showing comparative haziness of cornea.

**Figure 8.8c**
Slitlamp view of epikeratophakia for keratoconus showing double light scattering from Bowman’s layer.
seven patients who had undergone epikeratophakia for keratoconus, but who had subsequently required penetrating keratoplasty. The reasons for epikeratophakia failure were poor vision, caused chiefly by scarring in the lenticules from epithelial problems, or scarring in the underlying host tissue. All the patients achieved 6/12 or better acuity following penetrating keratoplasty and all the grafts were clear. There were rejection episodes in three of the seven cases (43%). In two of these cases the graft bed had become vascularised which made them at greater risk of rejection, but the series was regarded as too small to determine whether the epikeratophakia graft had significantly modified the prognosis.

A summary of the current relative indications and contraindications for epikeratoplasty in keratoconus are given in the box.
INTRODUCTION TO EPIKERATOPHAKIA

Treatment of keratoglobus and other tectonic indications

Maguen and Nesburn (in Los Angeles)\(^{61}\) described a case of bilateral keratoglobus with fluctuating vision. The patient's corneal thickness was 0.30 mm centrally, and varied between 0.29 mm and 0.40 mm peripherally. Initially, a conventional epikeratophakia procedure was attempted but this was aborted following perforation of the cornea at the time of trephination. Subsequently, a larger 12 mm graft was placed in an 11 mm bed (preoperative horizontal corneal diameter 12.75 mm). A similar procedure was carried out on the second eye and both eyes corrected to 6/7.5 postoperatively with a stable refraction.

Pellucid marginal corneal degeneration is a corneal ectatic degeneration characterised by stromal thinning, most commonly in the inferior paralimbal region. This typically produces peripheral corneal steepening, and high degrees of against the rule irregular myopic astigmatism. In 1991 Frøntrè and Portesani reported two cases treated by epikeratophakia.\(^{16}\) They used systemic and topical hypotensive agents both intraoperatively and postoperatively. As a result of the peripheral nature of the ectasia, they found 12 mm diameter grafts most satisfactory, or alternatively recommended an 11 mm graft slightly decentred inferiorly.

Epikeratophakia for paediatric aphakia

Development of epikeratophakia in children was in the hands of the paediatric ophthalmologist at Louisiana State University, Keith Morgan. His first report of paediatric epikeratophakia in 1981 gave results of 17 patients with monocular congenital or traumatic cataracts.\(^{62}\) Somewhat characteristic of the approach adopted was that the first paediatric epikeratophakia patient underwent combined epikeratophakia with penetrating keratoplasty and lensectomy. This procedure failed, as did a total of seven of the 19 grafts in the series. Half of the children had epikeratophakia as a primary procedure combined simultaneously with cataract extraction. In the early part of the series a tarsorrhaphy was carried out to help protect the graft, but this was found to be counterproductive and bandage contact lens wear was adopted instead. The tendency for the children to rub their eyes was tackled by splinting their arms. The eye was further protected by fixing a shield over it without a pad and applying ointment through the holes in the shield. After suture removal at three weeks, aggressive occlusion therapy was instituted, rapidly building up to 90% of waking hours in preverbal children. In the verbal child 100% occlusion was used, as the acuity in the unoperated eye could be
A refractive undercorrection was generally obtained with the successful grafts. The lenticules were said to be cut according to the theoretical parameters of Werblin and Klyce, although this was contradicted some years later. It was noted that, although the mathematical model predicted that up to +50 D of change could be obtained, in clinical practice they were unable to achieve more than +14 D in any case. This led to modification of the surgical technique by changing the graft-bed diameter disparity from 0.5 mm to 2.0 mm. The continuous suturing technique was also changed to that of interrupted suturing.

Two and a half years follow up of 50 grafts in 47 children was presented by Morgan et al in 1983. This report recorded changes in the tissue preparation technique, some of the lenticules being lyophilised rather than stored in liquid nitrogen. The final eight grafts were prepared with donor tissue hydration control before lathing, and the lathing was carried out with compensation for thermally induced dimensional changes. In spite of these changes, there were still wide fluctuations in the accuracy of dioptric correction achieved, with ranges of +9.00 D to -12.50 D of over- and undercorrection in the first 22 cases, and from +6.50 D to -9.00 D in the subsequent eight cases in which pressed tissue was used. The surgical technique remained unchanged from the state to which it had evolved in the previous report. Postoperative management now included prophylactic oral amoxycillin from the time of surgery to suture removal. With the larger numbers and longer follow up time, a number of spectacular successes were presented, including a child with a congenital cataract who had achieved 6/18 Snellen equivalent, and a three year old child with traumatic cataract who recovered 6/9 with fusion and stereopsis to a level of 400 seconds of arc.

By 1984 Morgan had operated on 61 children and reported the results of 54 grafts with more than six months of follow up. Criteria for surgery were documented as changing from “largely on children for whom this surgery was a last resort” to being offered as “an optional alternative to contact lenses to parents of children undergoing cataract extraction”. The overall proportion of combined cataract and epikeratophakia versus secondary epikeratophakia grafts on aphakic eyes was now around 40% compared with the 50% in the earlier reports. Analysis of the visual results was by now showing better acuities in those with acquired rather than congenital cataracts. Results in congenital cataracts were thought not to be strictly comparable with other series as a result of the heterogeneity of the cases selected.

In another publication in 1985, Arffa et al gave a further analysis of the refractive and keratometric results of the Louisiana State University paediatric series. This paper brought out clearly the tendency for refractive undercorrection of children having epikerato-
phakia during the first year of life, with only three of 14 children less than one year of age at the time of surgery achieving within 3 D of emmetropia, with average postoperative refraction of $+6.92 \pm 4.67$ D. In the light of this the authors suggested that epikeratophakia should no longer be recommended as the initial refractive treatment of congenital cataracts, but should be offered as a secondary procedure only in contact lens intolerant children older than one year of age. In the one year age group 35 of 54 patients (65%) were within 3 D of emmetropia with average postoperative refraction $-0.72 \pm 4.22$ D. Selecting only the most recent 34 cases from this group gave an improved figure of 71% (24/34) within 3 D of emmetropia.

A further analysis of the long term changes following epikeratophakia was presented by Arffa et al in 1986. They noted that there was little average change in keratometry over time, being 2 D over three years. This change was even lower in older children. Although up to 8 D of keratometric change was observed in two children, two thirds were within 2 D of their initial readings. Gordon and Donzis found, in normal children, a decrease in keratometry of 1·6 D between six months and three years, and 0·5 D between two and four years. This was slightly less than that observed in the epikeratophakia patients (2·0 D and 0·8 D respectively). Changes in refraction were more significant: after two years patients having surgery at less than one year of age had become 4.21 D more myopic, whereas patients greater than one year at surgery became 1.80 D more myopic. It was postulated that some of the development of myopia may be related to visual deprivation or amblyopia, but they could not find any significant association between visual outcome and degree of refractive change.

The multicentre trial of paediatric epikeratophakia

The first review of patients treated outside Louisiana as part of Allergan's multicentre study came in 1986 from Kelley et al at Ohio State University. All patients were aphakic and contact lens intolerant, so this was the first report of a series of entirely secondary epikeratophakia procedures. This study included 11 children, but only seven of these were less than eight years old with the youngest aged nine months. Refractive correction fell within 3 D of emmetropia in all cases. The authors noted successful re-epithelialisation in all 11 cases within one week of surgery without the use of bandage contact lens or tarsorrhaphy, using only a simple eye shield and topical ointment application. Subsequently a report from Uusitalo and
Lehtosalo (Helsinki) on 18 children had all cases within 2 D of emmetropia apart from one graft failure.\textsuperscript{72}

A full report on the multicentre trial also appeared in 1987,\textsuperscript{73} 97 surgeons participated in this trial and carried out 335 grafts in children (here defined as less than eight years of age). Forty five of the 335 (13\%) were combined epikeratophakia and cataract extraction (primary procedures). Thirty six grafts had to be removed, but 21 were regrafted, giving an overall retention rate of 95\%. The most common cause of graft failure was epithelial defect. Seventy three per cent of patients achieved corrections within 3 D of emmetropia. Three grafts were removed as a result of poor refractive correction. Twelve cases were operated on in the first year of life without the large degrees of undercorrection documented in previous reports. This was attributed to the fact that the average age at surgery (7-6 months) was greater than in previous studies, or alternatively to improved lathing technique. In the light of earlier long term studies, however, it was pointed out that these infants were likely to become significantly myopic with longer follow up. With only a limited follow up time, visual results were not fully documented but the traumatic cataract subgroup (average age 5-2 years) again showed favourable results in comparison to alternative techniques.

Morgan's review in 1986\textsuperscript{4} included 88 patients. The average postoperative refraction was +0.56 D, although in the less than one year age group it was +5.76 D. If this group was excluded the average refractive error was −0.73 D with a range from −10.50 D to +10.38 D. Results of long term follow up of refractive change showed an average loss of 1.5 D per year, this figure being much higher in those operated on during the first year of life. Keratometric measurements also showed a myopic shift of around 0.5 D per year. There were 20 graft failures and no changes whatsoever were noted in the corneal curvature as a result of the failed graft surgery, and only one of the 20 developed significant corneal scarring. The results from children with incomplete congenital cataracts were good, with visual improvement in every case. Morgan considered that the traditional indications for surgery in this group should be re-evaluated.

A further report in 1990 from Uusitalo\textsuperscript{7} detailed a group of children with unilateral congenital cataract treated with epikeratophakia; 14 of 15 grafts were successful and an acuity of 6/60 or better achieved in three of 11 patients with dense cataracts. All the children with incomplete cataract obtained good acuities ranging from 6/30 to 6/9. Almost all of the cataracts had been diagnosed late (greater than three months old) and combined with the subsequent development of contact lens intolerance were a group with an intrinsically poor prognosis. Uusitalo concluded that the results obtained were comparable to those achieved with contact lenses.
Epikeratophakia for traumatic cataract

In 1985 Morgan reported a series of six cases of traumatic cataract with epikeratophakia. Children selected in this study had traumatic cataracts and corneal laceration in excess of 3 mm in length, with exclusion of those requiring penetrating keratoplasty and those with follow up of less than six months. Five of the six grafts were successful and these cases all achieved 6/12 or better corrected acuities. Epikeratophakia was considered particularly useful for traumatic cataracts because irregular astigmatism associated with the corneal laceration was said to be masked by the graft. The visual results obtained were considered favourable compared with other series, especially for the children under four years of age, where acuities of 6/60 had rarely been obtained before.

Vila-Coro and Goosey and colleagues from Houston, Texas reported a series of four patients with traumatic cataract that they treated with epikeratophakia. The lenticules were prepared in their own laboratory by cryolathing, but were not lyophilised. All four cases were successful, with best corrected postoperative acuities ranging from 6/9 to 6/24. The least successful postoperative acuity was attributed to amblyopia and failure to comply with patching therapy. The best case (6/9) also underwent rotational autokeratoplasty to remove scars from the visual axis. It was felt that, in the remaining cases, the visual recovery was less than 6/6 as a result of residual scarring close to the visual axis.

Ten year perspective

An overview of the management of paediatric aphakia by epikeratophakia was presented by the Louisiana State University workers after some ten years of experience with the procedure. Indications include both aphakia, and congenital or acquired cataracts in children older than one year. Contraindications include blepharitis, dry eyes, and lagophthalmos. It was recommended that lenticule power for combined cataract and epikeratophakia procedures should be calculated with the Donzis–Kastl–Gordon intraocular lens implant formula following ocular biometry.

Current postoperative management recommendations include: a bandage contact lens worn continuously under a clear plastic eye shield with holes, and treatment with topical and oral antibiotics continued until suture removal at 2–3 weeks. Occlusion therapy is usually started within one week of suture removal, beginning with three hours per day, and increasing per day up to 95% of the child’s
waking hours. Spectacle correction with executive bifocals is usually prescribed 3–6 months after surgery. The current indications and contraindications for epikeratophakia for paediatric aphakia are given in the box.

### Indications for paediatric epikeratophakia for aphakia

**Indications**
- In aphakia with contact lens intolerance
- In unilateral cataract when contact lens intolerance is anticipated
- In traumatic cataract or aphakia when anterior segment damage contraindicates intraocular lens implantation

**Contraindications**
- In infants less than one year old
- Where there is likely to be irreversible amblyopia, or failure to comply with occlusion therapy
- Where there is lagophthalmos, blepharitis, poor tear film, or previous radiotherapy that is likely to give rise to poor epithelial stability

### Correction of aphakia in adults

In 1981 Werblin first reported results of epikeratophakia for the correction of aphakia in adults in a small randomised comparative trial of epikeratophakia compared with keratomileusis. Secondary intraocular lens implants were not being carried out in Louisiana State University at that time. Analysis of results from 14 patients showed that epikeratophakia was at least as good as homoplastic keratomileusis, and the protocol was changed so that subsequently all patients received epikeratophakia grafts.

In the same year Werblin published the results of the first 21 patients which showed a significant tendency towards undercorrection, the first 16 patients having an undercorrection of $+5.4 \pm 0.9$ D. This prompted revision of the lathing parameters and modification of the surgical technique, including increasing the graft-bed diameter disparity to 1.5 mm. As a result of these modifications, an increase in accuracy of refractive correction was found in the final five cases of the series.

By 1983 the series had been extended to 65 cases with 31 patients having more than four months of follow up. The residual refractive error in those with follow up for more than one year was about 3.5 D, whereas it was only about 1.5 D in the rest of the group. The
improvements in accuracy were attributed to the introduction of the corneal press to control corneal thickness before lathing, and to the development of the technique for compensating for thermally induced dimensional changes on the cryolathe.

Multicentre trials

The first report of results using commercially prepared lenticules was presented by Arffa et al in 1986. This covered patients at Louisiana State University having surgery between February 1984 and November 1985. All but one patient was unilaterally aphakic. The first 14 patients in the series had a 1.5 mm graft-bed disparity with wedge resection only, but the second 26 eyes (after September 1984) had the addition of a peripheral lamellar split. There was not, however, any significant difference in the refractive results between these two subgroups. Overall, in those with three months of follow up 29% were within 1 D of emmetropia, and 90% within 3 D. The remaining three patients were within 5 D; 37 of 40 eyes maintained clear grafts. One was removed as a result of recurrent epithelial defects, one because of graft haze, and one because of focal opacification.

McDonald et al reviewed the results of the multicentre epikeratophakia trial for adult aphakia in 1987. This report covered 310 patients with a minimum of one month of follow up after suture removal. In the analysis of results, various subgroups of less than 310 patients were presented without clear definition of how the subgroups were derived. With regard to dioptic correction, in 229 patients 75% were within 3 D of emmetropia. Individual results were not numerically presented but, from the scattergram, the range appears to extend from -6.5 D of overcorrection to +13 D of undercorrection. The change in best corrected Snellen line acuity was analysed by age at the time of surgery. This showed that 97% of those under 70 years old, 83% of 71–80 year olds, and 35% of 81–87 year olds achieved within one line or better of the best preoperative corrected acuity. This declining success with increasing age was also reflected in an increased incidence of loss of three or more lines of best corrected acuity, which was attributed to posterior capsular opacification in some, or thought to be possibly related to retinal dysfunction.

Comparison with secondary intraocular lens implants

Durrie et al (in Omaha, Nebraska, USA) carried out a comparative trial of epikeratophakia and secondary intraocular lens implantation
reported in 1987. Patients were not randomised to the two treatments because it was felt that there were distinct clinical indicators to determine the appropriate procedure. Patients were regarded as unsuitable for secondary intraocular lens implantation if they had chronic iritis, a disorganised anterior chamber, endothelial cell count of less than 1000/mm², or age under 40 years. Thirty consecutive secondary intraocular implants were compared with 30 consecutive epikeratophakia grafts, all operations being performed by one surgeon. Six different types of implants were used, but in 21 of the cases it was a Stableflex (Optical Radiation Corp). At follow up of at least six months, 87% of the implant group were within 2D of emmetropia compared with 70% of the epikeratophakia group. BCVAs were generally better in the implant group although there were a few with significant complications including uveitis–glaucoma–hyphaema syndrome, cystoid macular oedema, and pseudophakic bullous keratopathy. Complications also occurred in the epikeratophakia group with four patients requiring graft removal. Following removal, however, a satisfactory replacement graft was undertaken in every case.

Hoffer subsequently pointed out that the Stableflex lens had been “essentially withdrawn from the market” by its manufacturer and suggested that other comparative trials should be conducted comparing the results with different anterior chamber lenses.

Visual recovery following epikeratophakia or secondary lens implantation

Bates et al, in a report published in 1991, compared the rates of visual recovery of patients undergoing epikeratophakia with a retrospective examination of patients who had secondary implants. At six months after the operation, 95% of the secondary implant group saw 6/12 or better, compared with 72% of the epikeratophakia group. An acuity of 6/9 or better was achieved by 67.5% of the secondary implant group compared with 64% of the epikeratophakia group. These figures compared earlier reports of delayed visual recovery following epikeratophakia and, although epikeratophakia is clearly the procedure of choice for surgical correction of aphakia in cases where there is a disorganised anterior segment, chronic inflammation, or a poor endothelium, in other cases where secondary lens implantation is an alternative the pattern of visual recovery following epikeratophakia is a factor to be considered in the choice of appropriate management (fig 8.9).
Harper et al, in 1989, reported contrast sensitivity following correction of aphakia by epikeratophakia, contact lenses, or intraocular lens implants. It was found that, in spite of relatively good visual acuity and satisfactory surgical results, there was a marked reduction of contrast sensitivity in the epikeratophakia and contact lens correction eyes. Glare accentuated the loss of sensitivity especially in the patients with epikeratophakia. Lass et al (in Cleveland, Ohio, USA), in a small personal series of 12 cases published in 1987, achieved only 50% within 2D of emmetropia with a range from -4.5D to +2.5D. In 1989, Wagoner and Steinert published the

Figure 8.9
Epikeratophakia for aphakia following perforating injury: although the graft has corrected the refractive error, the eye is still photophobic, necessitating pupilloplasty.
results of a series of 21 eyes undergoing epikeratophakia using American Medical Optics (AMO) lenticules. They achieved 74% within 3 D of emmetropia with a range of −4.5 D to +4.5 D; 17 of the 21 patients (81%) expressed subjective satisfaction and were considered functionally successful.

The current indications and contraindications for epikeratophakia for adult aphakia are given in the box opposite.

**Figure 8.10**
Epikeratophakia exchange: an aphakic eye with an epikeratophakia graft complicated by an epithelial island at the graft–host interface (grey patch to right of pupil); here the graft is being removed six months postoperatively. The peripheral lamellar split is opened with a sweeping motion of a forcep tip, and the graft peeled off. The graft was exchanged for a new lenticule as a result of initial undercorrection. Final acuity was 6/9 unaided with refraction plano, +0.5 D Cyl × 180°.
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**Indications**
- Aphakia with contact lens intolerance, especially where there is a disorganised anterior segment, previous uveitis, glaucoma, or a poor endothelial cell count
- Younger patients
- When the patient prefers a low risk intervention

**Contraindications**
- Dry eyes, blepharitis, or lagophthalmos
- Old age with poor wound healing
- Where trauma has caused mydriasis and photophobia, and pupilloplasty is going to be carried out, giving the option of simultaneous intraocular lens implantation if this is feasible
- Where the corneal endothelium is on the verge of decompensation, and penetrating keratoplasty is likely to be needed, which could be combined with secondary intraocular lens implantation

**Correction of myopia**

In 1981 Kaufman’s team had already started clinical trials of epikeratophakia for aphakia and keratoconus, and in a review of keratorefractive procedures he put forward the possibility of also using the technique to correct high myopia.\(^3\)

Werblin et al were to publish theoretical papers on lathing parameters for manufacture of myopic epikeratophakia lenticules,\(^4\)\(^5\) but the first published report of experimental myopic epikeratophakia did not appear until 1984, from workers in San Diego.\(^6\) They had performed epikeratophakia in a baboon and, although their hypermetropic grafts had achieved significant corneal steepening, they were disappointed to find that their two “myopic” grafts designed to give \(-10.0\) D of corneal flattening both achieved \(+10.4\) D of corneal steepening. This gross unpredictability was attributed in part to problems of digitising the corneoscope photographs, but also to lack of an appropriate computer program for the lenticule lathing.

In the same year the first clinical results of 11 myopic patients with preoperative refractions ranging from \(-8\) D to \(-21\) D were published by Kaufman.\(^7\) Postoperative results in eight of these cases ranged from \(+1\) D to \(-6.25\) D, but no individual data were presented. In response to the poor predictability of the refractive results, there were repeated changes of the lenticule design and surgical technique with modification of the graft-bed diameter disparity. In this study
published in 1985, in a series of 22 eyes, the graft–bed diameter disparity was 1.5 mm for the first six patients, 1.0 mm for the next four, and 0.5 mm (8.00 mm graft into a 7.50 mm bed) for the remaining ten. No peripheral lamellar dissection was performed. The first ten patients had poor visual results, with three grafts requiring removal, and an average undercorrection of $-6.0 \pm 3.88$ D. With the subsequent group of grafts with 0.5 mm disparity, the undercorrection averaged $0.38 \pm 2.80$ D. It was, however, felt that the 0.5 mm graft–bed disparity was more likely to cause folds in the recipient’s Bowman’s layer.

In the same year an excellent paper was published by Suarez et al on experimental myopic epikeratophakia carried out at Louisiana State University. Twelve African Green monkeys had myopic epikeratophakia grafts in both eyes, with six different groups made up of three pairs. Each pair had one eye operated on using the conventional surgical technique (0.5 mm graft–bed diameter disparity), whereas the other had the new technique of 1.5 mm graft–bed disparity, combined with peripheral lamellar splitting. The three groups received lenticules with calculated powers of $-10$ D, $-20$ D, and $-35$ D. The rationale behind the new surgical approach was that it was felt that the existing technique of inserting an 8 mm graft into a 7.5 mm bed necessitated excessive suture tension to be able to abut the lenticule margin with the edge of the host tissue in the wedge resected bed. This caused compression of the host cornea with folding and flattening of the lenticule wing, with resultant undercorrection. The new operative technique employed an 8.5 mm graft into a 7.0 mm bed (1.5 mm graft–bed disparity). In addition, a peripheral split was made from the bottom of the wedge resection. This allowed the lenticule to be fixed in place without creating undue tension in the tissue which might alter the refractive effect. The results confirmed Suarez’s theory and showed significantly enhanced accuracy and completeness of refractive correction. The paper undoubtedly made a major contribution to the development of epikeratophakia in its recognition of the effect that excessive suture tension and the graft–host junction configuration have on refractive outcome.

In spite of the variation in technique, it was still possible to obtain good results using the early 0.5 mm graft–bed diameter disparity. Two cases written up by Keates et al achieved excellent vision in spite of previous surgery.100 The first patient had previously undergone failed radial keratotomy ($-8.75$ D Sph, $+1.0$ D Cyl $\times 50^\circ$ pre-RK, $-7.0$ D Sph $+1.25$ D Cyl $\times 50^\circ$ post-RK), and with an epikeratophakia placed on top of the radial keratotomy (RK) achieved 6/6 unaided vision with a refraction of $+0.75$ D Sph. The second patient had previously undergone bilateral penetrating keratoplasty for keratoconus, but was left with residual myopia of $-7.25$ D Sph, $+4.0$ D Cyl $\times 10^\circ$ right, and $-9.0$ D Sph $+7.0$ D Cyl $\times 40^\circ$ left. The
right eye received a specially prepared 9 mm diameter lenticule which was sutured into an 8.5 mm bed, placed around the existing 8 mm penetrating graft. After the operation, the unaided vision was 6/9 and refraction plano, +1.5 D Cyl × 155°. Thus, even in the most difficult circumstances, it was possible to achieve excellent results with the conventional technique.

By 1987 corneal topography had reached a state of development where it could be usefully applied to patients following kerato-refractive surgery. Studies by Maguire et al. showed that the effective optic zone following myopic epikeratophakia was smaller than theoretically predicted, and often centred. Another problem with myopic epikeratophakias becoming apparent at that time was progressive loss of refractive power. Although axial myopia does undoubtedly progress in some patients, loss of refractive effect was documented even in eyes with stable axial length. Both these findings were interpreted as suggesting that the effect of wedge keratectomy was deleterious to refractive outcome and that the 1.5 mm oversize lenticule in a bed with no keratectomy would give better results.

The results of Allergan's multicentre trial of myopic epikeratophakia lenticules were published in 1987. This report covered all operations performed between 1983 and December 1985. Of 256 patients who had follow up of at least one month after suture removal, there were 201 patients who had 8.0 mm graft/7.5 mm bed/keratectomy/no lamellar dissection, and 55 who had the modified 8.5 mm graft/7.0 mm bed/keratectomy/lamellar dissection. BCVA was improved in more than 25% of the patients, but refractive accuracy was still poor, with 86% of the patients within 4 D of emmetropia. Ten per cent of grafts required removal, resulting mainly from poor acuity or persistent epithelial defects, and one patient subsequently required a penetrating keratoplasty. In 1987, Colin from Brest, France published a resumé of the 352 patients who had myopic epikeratophakia on the multicentre trial, giving 75% within 3 D of emmetropia with 33% of those patients obtaining an uncorrected acuity of 6/12.

As Allergan's myopic epikeratophakia trial gave such variable results, the FDA withheld approval, and so Allergan ceased distributing epikeratophakia lenticules for myopia. Further development of the technique came from surgeons using other methods to manufacture their own lenticules. In 1987 Krumeich and Swinger reported the first series of myopic epikeratophakia grafts carried out with lenticules prepared using the BKS 1000 (Barraquer-Krumreich-Swinger) equipment. The series consisted of 23 procedures in 18 patients with follow up from one month to two years. Postoperative keratometric change was found to be on average
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about half the value of the spectacle refractive change. Mean postoperative spherical equivalent was $-3.0 \pm 3.0$ D at one month, and $-0.2 \pm 2.5$ D at one year. They found little significant change in refraction between two months and one year of follow up. They used a 9 mm lenticule sutured into a 7 mm bed with 0.7 mm undermining. One patient had reoperation for overcorrection, but there were no other significant complications.

Management of overcorrection

Three cases of overcorrected myopic epikeratophakia grafts were presented in 1988 from the University of Minnesota, Minneapolis by Nichols et al. These patients had AMO lenticules with 1.5 mm graft-bed diameter disparity placed into peripheral splits without keratectomy. Postgraft refractions were +9.37 D, +2.25 D, and +5.25 D. The overcorrection was treated by resuturing of the wound following surgical dehiscence, carried out under keratometric control. Postoperative refractions were all within 1.5 D of emmetropia. The complete series of their seven myopic cases was presented by the Minnesota team the following year, showing a general tendency to overcorrection with their technique.

Another series of seven myopic patients reported from Massachusetts by Wagoner and Steinert had generally poor results. They attempted to quantify “success” of myopic grafting as the following: stable refractive error, UCVA within two lines of best corrected preoperative acuity, and corrected acuity within one line of best corrected preoperative acuity. By these criteria only 43% of their cases were successful. In addition three cases showed marked refractive regression postoperatively, and one eye developed host corneal opacification after two failed grafts.

A view to the future

As a minimally invasive and potentially reversible procedure, epikeratophakia at the outset had every indication of taking a major role in the correction of refractive error. After 15 years of research and development, the initial enthusiasm has somewhat waned and the procedure is seen in some respects to have failed to deliver the goods promised. Epikeratophakia for keratoconus has certainly gained acceptance, giving the best results when it is used early in the disease process, but is still struggling against a long standing
attitude that keratoconus should be treated surgically only in its advanced stages. Epikeratophakia for hypermetropia and myopia has yet to become generally accepted because of poor predictability of refractive outcome.

How is it that contact lens manufacturers can produce lenses by the million with perfect optical predictability, and yet epikeratophakia lenticules produce such variable results? The answer must lie primarily in the variability of the donor corneal material used to make the lenticules. Contact lens manufacturers achieve their results only by going to great lengths to maintain consistency in the quality of their raw materials. Little is known of how to select, analyse, or standardise donor tissue for epikeratophakia.

The “simple” alternative of making a synthetic epikeratophakia lenticule has been tackled by a number of workers, particularly the group in France. They have prepared synthetic lenticules from type IV human placental collagen, and these have been shown to be biocompatible and well tolerated as interlamellar inlays. When the synthetic material is used for epikeratophakia, the chief problem has been lack of stability of the epithelium over the lenticule. It is hardly surprising that corneal epithelium is unstable on a synthetic matrix when epithelial instability is also seen on human corneal lenticules. The following are important factors underlying this problem:

1. Development of normal hemidesmosomal attachments and anchoring fibrils for the basal epithelial cell layer
2. Mechanical stresses on the epithelium caused by the abnormal corneal contour
3. Trophic changes in the epithelium resulting from absent innervation.

The ideal epikeratophakia lenticule can thus be seen to require a topographic configuration that meets both optical and biomechanical demands, has a surface that favours anchoring of epithelial cells, and a substrate compatible with re-innervation. At present the materials that most nearly fulfil these last demands are normal human Bowman’s layer and human corneal stroma, and it seems likely that a biosynthetic alternative that even matches these characteristics, let alone exceeds them, is a long way off.

There have been reports that the use of biosynthetic epidermal growth factor expedites the re-epithelialisation of epikeratophakia grafts. Such pharmacological modification of the postoperative wound healing process may hold the key to increasing the success of epikeratophakia surgery and allow synthetic lenticules to be employed, but licensing of such drugs for clinical use is awaited.
Arguments against using donor human corneal tissue revolve around the availability of donor material and risk of infectious disease transmission. If a synthetic alternative is to be satisfactory, it seems likely that it would have to be entirely biosynthetic or at least derived from animal sources to reduce the risk of disease transmission. The collagen used in the manufacture of the lenticules tested by the French workers is, however, derived from human placentas, and the risk of disease transmission is compounded by the fact that the material from many donors is pooled to make the basic substrate. With this method of manufacture, even the most stringent measures to counteract viral transmission may still leave doubt as to the safety of the product.

During the development of epikeratophakia many unsolved problems and unanswered questions have arisen, but in its first 15 years there have been triumphs as well as setbacks. If one considers the first 15 years of the development of intraocular lenses, there was enthusiasm from the pioneers and gratitude from patients with unprecedented rehabilitation from their handicap, but there were also many disasters along the way, and the ophthalmic profession was generally sceptical about the concept. Thirty years on, and mainstream ophthalmology has been revolutionised by the intraocular lens. Who knows what the next 30 years will hold for epikeratophakia?

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