EXTENDED REPORT

Amniotic membrane transplantation for ocular disease: a review of the first 233 cases from the UK user group

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Background: Amniotic membrane transplantation (AMT), as a new tool in the armamentarium of therapies available for ocular surface problems, became widely available in the UK in 1998. This study evaluates the indications for treatment, the surgical procedures used, and the results of a subset of the first AMT cases carried out by the group using this nationally available supply. This user group model provides data which is different from that obtained from uncontrolled case series, or clinical trials, and may be more representative of the outcomes that can be expected when a procedure becomes widely available.

Methods: The first 233 AMTs, performed by the UK user group, were evaluated by audit and outcomes were assessed at 3 months.

Results: Of the 233 transplants, there were 126 (54.1%) valid outcome returns: the outcome for persistent epithelial defects was a healed and stable surface in 11/35 (31.4%, 95% CI 16.9 to 49.3); for chemical/thermal injuries, a healed uninflamed eye with clear cornea in 5/18 (27.8%, 95% CI 9.7 to 53.4); for bullous keratopathy a pain-free, stable surface without bullae in 4/18 (22.2%, 95% CI 6.4 to 47.6); for ocular surface reconstruction, an epithelialised uninflamed conjunctiva without scarring in 12/23 (52.2%, 95% CI 30.6 to 73.2); and for limbal stem cell deficiency, a corneal phenotype in 4/7 (57.1%). The operative technique least associated with failure was use of a bandage contact lens at the end of the procedure (OR 0.19, 95% CI 0.06 to 0.59, $p=0.004$). Previous treatment with topical steroids was significantly associated with failure (OR 5.70, 95% CI 1.77 to 18.43, $p=0.004$).

Conclusion: Although the outcome criteria used in this study were stringent, and the follow-up duration was short, the results of AMT by this user group were generally less favourable than those of previously reported case series. Controlled clinical trials would improve the quality of evidence for use of amniotic membrane in ocular disease.

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Amniotic membrane transplantation (AMT) in ocular surgery has now become widespread, and the number of clinical situations in which it has been applied has rapidly expanded.^{1–3} Whilst much has been published on its use in persistent epithelial defects (PEDs) and corneal perforations,^{4–6} limbal stem cell deficiency (LSCD),^{7–12} bullous keratopathy (BK),¹³ conjunctival reconstruction following excision of neoplasia,^{14–15} pterygia^{16–18} and for reformation of fornices^{19–21} as well as in acute ocular burns,^{22–24} the evidence base for use of amniotic membrane (AM) is not strong and there are only three randomised controlled clinical trials evaluating the effectiveness of AM, for pterygium surgery, acute ocular burns and neurotrophic ulcers.^{18–24–25} The remaining reports are case series, describing use of AM by a single specific method. How the results from these case series translate into clinical outcomes, when AM is used by multiple clinicians at multiple sites, is unknown.

There is also variability in the AM preparation technique used between the different case series. In some reports the Tseng method⁵ of AM preservation is used while in others the method described by Tsubota¹² is employed; in some reports hypothermically stored, and unpreserved,^{20–26} rather than cryopreserved AM is used.

In 1998 the North London Tissue Bank (NLTB) was approached to set up a supply of AM that would be available nationally, using a modification of the Tseng cryopreservation method.⁵ The method involved storage of the amnion at -80°C in 50% glycerol in Hanks' balanced salt solution. This technique

allowed sufficient storage time for the donor to be recalled and retested for the mandated microbiological markers, which would not have been possible with the shorter 4°C storage method. It also allowed for stock management of the amnion with resultant greater availability, whilst clinical outcome did not alter.²⁶ Over the period of the study, only minor adjustments were made to the processing method; assessment of cell viability was only undertaken during the validation period to ensure that the method rendered cells non-viable, after which it was discontinued and the initial 12-month storage duration was extended to 24 months from early on in the study. Various sizes of membrane were made available.

Corneal surgeons in the UK were advised of the availability of AM and were invited to join the Amniotic Membrane Transplant User Group (AMTUG) and participate in a study of AMT, by multiple ophthalmic specialists, using this single source of allograft. Following two reorganisations of the overarching organisation, the AM supply for ophthalmic use is now provided by NHS Blood and Transplant Tissue Services, although the initial development work was carried out in what was previously known as NLTB.

Abbreviations: AM, amniotic membrane; AMT, amniotic membrane transplantation; AMTUG, amniotic membrane tissue user group; BK, bullous keratopathy; BM, basement membrane; CHEM, chemical/thermal injury; LSCD, limbal stem cell deficiency; NLTB, North London Tissue Bank; OSR, ocular surface reconstruction; PED, persistent epithelial defect; TRAB, trabeculectomy.

Between June 1998 and December 2002 we distributed data collection forms, with the help of the NLTB, investigating the indications, operative technique and outcomes of the first 233 AM transplants performed by the user group. The purpose of this study was three-fold: first, to assess the impact (in terms of numbers of cases and indications for treatment) of this new technique in clinical ophthalmic practice in the UK; secondly to evaluate the methodology in use; and thirdly, to assess outcomes for treatment so as to provide a foundation for planning either audits or collaborative controlled clinical trials of AMT in the future.

METHODS

Between June 1998 and December 2002 an AMTUG study registration form was included with all AM transplants prepared by the NLTB. Surgeons were invited to register their patients in the study and become members of AMTUG. A data collection form detailing the indications, previous treatment, operative techniques and ancillary procedures was completed at initial registration. The outcome at 3 months postoperatively was assessed by a follow-up data sheet (see online Appendix 1 for the data collection forms <http://bjo.bmj.com/supplemental>).

When completing the data collection form, surgeons were instructed to indicate all options relevant to that case. In the operative technique section, use of the membrane was described as follows:

- As a graft with the basement membrane (BM) side up (either sutured within the defect with the edges buried under the epithelial source, or edges within both the epithelial defect and the limbus)
- As an overlay patch with the BM side up (eg over a persistent epithelial defect),
- As a mechanical bandage (eg over a trabeculectomy bleb or corneal perforation).

- As an anti-inflammatory patch (eg in chemical burns).

Whether the BM side was up or down was entered in a separate field.

The definitions of outcomes, for each indication, are given in Table 1.

Following initial registration of patients, at least two attempts were made by our research coordinator to increase the number of follow-up questionnaires received, through direct contact with individual members of the group.

Statistical methods included multiple logistic regression to assess risk factors for poor outcome, and estimation of proportions using exact procedures to compute 95% confidence limits.

RESULTS

During the study period, 233 procedures were registered and performed on 192 patients. 163 (85%) of the 192 patients had a single procedure, 40 (21%) required two procedures, 18 (9%) required three and 12 (6%) required four procedures. Of the 233 procedures, 141 (60.5%) completed three-month data collection forms were received, and 126 of these forms provided valid data, including outcomes relevant to the specified indications (54%). Surgeons at 34 collaborating centres registered to become a member of the AMTUG (see online appendix 2 <http://bjo.bmj.com/supplemental/>).

Patient characteristics

Patient ages ranged from 3–89 years, with a mean age of 51.6 years (SD 19.2). 113 patients (60%) were male and 75 (40%) were female.

Indications

The indications for AM transplant, number of procedures for each indication and duration of treatment prior to transplantation are shown in Table 1. Neurotrophic keratopathy was

Table 1 Three-month outcomes specific to the main indication

PED Outcome	Description	n=35	%	Exact 95% CL
Satisfactory	Healed and stable surface	11	31.4	16.9 to 49.3
Intermediate	Almost healed surface	4	11.4	3.2 to 26.7
Failure	Not healed	20	57.1	39.4 to 73.7
LSCD Outcome	Description	n=8		
Satisfactory	Corneal phenotype	5	62.5	24.5 to 91.5
Failure	Conjunctival phenotype	3	37.5	8.5 to 75.5
OSR Outcome	Description	n=23		
Satisfactory	Conjunctiva epithelialised, not inflamed, no or minimal scar	12	52.2	30.6 to 73.2
Intermediate	Conjunctiva epithelialised, but scar or inflamed	11	47.8	26.8 to 69.4
Failure	Conjunctiva not epithelialised	0	0	0
CHEM Outcome	Description	n=18		
Satisfactory	No inflammation and corneal epithelium healed and stable and corneal stroma clear, and limbal ischaemia reduced or absent.	5	27.8	9.7 to 53.4
Intermediate	Some remaining inflammation or corneal epithelium only partly healed or some remaining corneal stromal haze.	4	22.2	6.4 to 47.6
Failure	Inflammation or corneal epithelium not healed or corneal stroma hazy or limbal ischaemia unchanged.	9	50.0	26.0 to 74.0
BK Outcome	Description	n=18		
Satisfactory	Pain free and no bullae and stable surface	4	22.2	6.4 to 47.6
Intermediate	Pain or bullae, but stable surface	6	33.3	13.3 to 59.0
Failure	Unstable surface	8	44.4	21.5 to 69.2
TRAB Outcome	Description	n=2		
Satisfactory	IOP controlled	1	50.0	1.3–98.7
Failure	IOP not controlled	1	50.0	1.3–98.7

PED, persistent epithelial defect; LSCD, limbal stem cell deficiency; OSR, ocular surface reconstruction; CHEM, chemical/thermal injury; BK, bullous keratopathy; TRAB, trabeculectomy

present in 19/88 patients (21.6%) in the persistent epithelial defect group. The severity of the burns was grade 1 in 7/18 (38.9%), grade 3 in 2/18 (11.1%), and grade 4 in 9/18 (50%).

43/233 procedures (18%) had two or more indications. Two cases had four indications (CHEM + PED + LSCD + OSR, $n = 1$), (PED + BK + LSCD + OSR, $n = 1$ of aniridia); 8 cases had three indications (CHEM + LSCD + OSR, $n = 3$), (PED + LSCD + OSR, $n = 3$), (CHEM + PED + LSCD, $n = 2$); and 33 cases had two indications (including 2 aniridia cases having both LSCD and requiring ocular surface conjunctival reconstruction (OSR)). Of the 88 cases with PED 67 (76%) had PED alone, 12 (14%) were associated with LSCD, 10 (11%) were associated with OSR, 6 (7%) were associated with a chemical or thermal burn (CHEM), and 2 (2%) were associated with BK. Of the 42 CHEM cases, 22 (52%) had CHEM alone, 13 (31%) were associated with LSCD, 8 (19%) were associated with OSR, and 6 (14%) were associated with a PED.

"Other" indications included Molteno tube exposure or erosion ($n = 3$), corneal perforation ($n = 2$), corneal protection for anaesthesia, thinning or postoperatively ($n = 4$), dellen ($n = 1$), and ichthyosis ($n = 1$).

Previous treatment

The treatment used prior to AMT, for each indication, is shown in online Appendix 3 (<http://bjo.bmj.com/supplemental/>). For persistent defects, previous AMT had been performed in 10/88 (11.4%), and more than one previous AMT in 3 cases. Botulinum toxin had been used in 6/88 (6.8%) & tarsorrhaphy

in 3/88 (3.4%). Treatment had been given for an average of 16.7 weeks (SD 26.3) prior to AM surgery. For bullous keratopathy, previous treatment had been given for an average of 33 weeks (SD 63.8), including therapeutic contact lens in 20/42 (47.6%) and PTK in 4/42 (9.5%).

Operative technique

Table 3 describes the operative technique used in the 233 registered cases. AM was most frequently used BM side up in 92/233 (39.5%) cases rather than stromal side up in 18/233 (7.7%). 10/0 nylon or vicryl were used most frequently, as interrupted sutures. A therapeutic contact lens was used in 110/233 (47.2%) of cases.

Postoperative treatment required

The postoperative treatment given for the 141 procedures for which follow-up data was received is shown in online Appendix 3 (<http://bjo.bmj.com/supplemental/>).

Outcome

The outcome at three months is summarised in table 1.

Factors associated with failure

Overall, there were 49 (39%, 95% CI 30% to 48%) failures out of 126 valid returns. Multiple logistic regression analysis using a stepwise inclusion/exclusion procedure identified a number of factors that were strongly associated with failure. These are summarised in table 4. Previous treatment with topical steroids

Table 2 Indications for amniotic membrane transplant

Indication	Number (%)	SE	Previous treatment duration in weeks (SD)
1. PED	88 (37.8)*	3.2	16.7 (26.3)
Neurogenic: herpes zoster/simplex	14 (15.9)†		
post-operative	7 (8.0)		
Trauma: chemical burns, artefacta	12 (13.6)		
Infection (1 with inflammation)	11 (12.5)		
Keratoconjunctivitis sicca (3 with inflammation)	9 (10.2)		
Inflammation: ocular cicatricial pemphigoid	9 (10.2)		
Stevens Johnson	2 (2.3)		
Other	10 (11.4)		
Lid anomalies (3 with inflammation or infection)	5 (5.7)		
Diabetic autonomic neuropathy	5 (5.7)		
Medicamentosa	3 (3.4)		
Epithelial basement membrane dystrophy	1 (1.1)		
2. LSCD	35 (15.0)	2.3	34.7 (67.9)
Total	21 (60.0) †		
Sectoral	10 (28.6)		
Mosaic	4 (11.4)		
3. OSR	67 (28.8)	3.0	33.1 (107.1)
Lesion excision (pterygium, neoplasia, other)	19 (28.4) †		
Conjunctival cicatrix	34 (50.7)		
Lesion excision and conjunctival cicatrix	2 (3.0)		
Other	12 (17.9)		
4. CHEM	42 (18.0)	2.5	4.3 (11.2)
Acid	3 (7.1) †		
Alkali	34 (81.0)		
Acid and Alkali	4 (9.5)		
Thermal	1 (2.4)		
5. BK	42 (18.0)	2.5	33.0 (63.8)
6. TRAB	2 (0.9)	0.6	16.0 (5.7)
7. Other	11 (4.7)	1.4	49.5 (156.1)
8. Unknown	2 (0.9)		
TOTAL	233		

PED, persistent epithelial defect; LSCD, limbal stem cell deficiency; OSR, ocular surface reconstruction; CHEM, chemical/thermal injury; BK, bullous keratopathy, TRAB, trabeculectomy

*% of 233 procedures. Total number of indications exceeds total number of procedures due to more than one indication per procedure; †% of cases within each indication

Table 3 Operative technique according to main indication

Operative Technique	PED n=88 (% of n)	LSCD n=35 (% of n)	OSR n=67 (% of n)	CHEM n=42 (% of n)	BK n=42 (% of n)	TRAB n=2 (% of n)	OTHER n=11 (% of n)	All Indications n=233 (% of n)
AM graft (BM side up) sutured within confines of defect	18 (20.5)	9 (25.7)	17 (25.4)	3 (7.1)	5 (12.2)	0	1 (9.1)	44 (19.0)
AM graft (BM side up) edges buried under epithelial source	4 (4.6)	2 (5.7)	3 (4.5)	2 (4.8)	4 (9.5)	0	1 (9.1)	12 (5.2)
AM (BM side up) edges within both limbus and epithelium	13 (14.8)	3 (8.6)	6 (9.0)	1 (2.4)	13 (31.0)	0	1 (9.1)	31 (13.3)
AM overlay patch (BM side up)	43 (48.9)	11 (31.4)	7 (10.5)	9 (21.4)	13 (31.0)	0	4 (36.4)	76 (32.6)
AM mechanical bandage	8 (9.1)	5 (14.3)	10 (14.9)	1 (2.4)	3 (7.1)	1 (50.0)	0	19 (8.2)
AM anti-inflammatory explant	4 (4.6)	6 (17.1)	3 (4.5)	13 (31.0)	0	0	1 (9.1)	16 (6.9)
AM other	5 (5.7)	1 (2.9)	9 (13.4)	1 (2.4)	0	0	3 (27.3)	16 (6.9)
ANCILLARY PROCEDURES								
Superficial keratectomy	8 (9.1)	7 (20.0)	13 (19.4)	6 (14.3)	9 (21.4)	0	0	36 (15.5)
Lamellar keratoplasty	2 (2.3)	1 (2.9)	3 (4.5)	1 (2.4)	0	0	1 (9.1)	5 (2.2)
Penetrating keratoplasty	4 (4.6)	2 (5.7)	2 (3.0)	2 (4.8)	0	0	0	8 (3.4)
Limbal stem cell allograft	2 (2.3)	3 (8.6)	3 (4.5)	2 (4.8)	0	0	0	6 (2.6)
Limbal stem cell autograft	1 (1.1)	2 (5.7)	1 (1.5)	3 (7.1)	0	0	0	4 (1.7)
Antimetabolites: mitomycin-C	0	0	0	0	0	0	0	0
Antimetabolites: 5-fluorouracil	0	0	0	0	0	0	0	0
Other ancillary procedure	14 (15.9)	1 (2.9)	12 (17.9)	4 (9.5)	5 (11.9)	1	4 (36.4)	39 (16.7)

AM, amniotic membrane; BM, basement membrane; PED, persistent epithelial defect; LSCD, limbal stem cell deficiency; OSR, ocular surface reconstruction; CHEM, chemical/thermal injury; BK, bullous keratopathy; TRAB, trabeculectomy.

appeared to be statistically significantly associated with failure. The operative technique least associated with failure was use of a bandage contact lens at the end of the procedure. Requiring a therapeutic contact lens after the initial postoperative period was significantly associated with failure. For the chemical/thermal injury cases, both grade 1 and grade 4 injury severity were associated with approximately 50% failure, although the numbers are small (table 5).

DISCUSSION

Indications

The most common indication for AMT was treatment of PED (88/233, 37.8%), followed by conjunctival repair for OSR (67/233, 28.8%), treatment of BK (42/233, 18.0%) and CHEM (42/233, 18.0%).

Outcomes

The outcomes for each indication are described below. Because of the study aims and design it is not possible to give a detailed analysis of case selection and all the ancillary procedures that may have contributed to the success or failure of AMT, as

would be done in a case series or clinical trial, although much of this data was collected and is presented with the results. However it was possible to carry out a limited analysis and the outcomes describe what happened to this patient group treated by a large number of different centres.

Persistent epithelial defect

A successful outcome with a healed stable surface at 12 weeks was only achieved in 31% (11/35) of PED, and 57% (20/35) remained unhealed. This compares poorly with previous studies reporting success rates of 70–91%^{4–6} where healing usually occurred within 4 weeks.

How this compares clinically with alternatives such as serum drops,²⁷ therapeutic contact lenses,²⁸ botulinum toxin-induced ptosis^{29–30} and tarsorrhaphy³¹ is unknown. 34.1% of the PED patients in this audit had already been treated with a therapeutic contact lens, and 13% with serum drops, without success. Although temporarily associated both with disfiguring appearance and visual compromise compared with AMT or therapeutic contact lenses, botulinum toxin-induced ptosis is reported to have a success rate of 76–90%.^{29–30}

Table 4 Factors associated with failure. Results from a final most parsimonious logistic regression model, after assessment and exclusion of all other non-significant factors using a step-wise procedure

Factor	Odds Ratio (95% CI for OR)	p-value
OSR (ocular surface reconstruction) required Referent: OSR not required	0.37* (0.17 to 1.30)	0.121
Previous Treatment: Topical steroids Referent: no topical steroids	5.70 (1.77 to 18.43)	0.004
Operative Technique: AM graft (BM side up, sutured within confines of defect) Referent: no AM graft	0.31* (0.07 to 1.28)	0.105
Operative Technique: Bandage contact lens Referent: no bandage contact lens	0.19* (0.06 to 0.59)	0.004
Operative Technique: AM anti-inflammatory explant Referent: no AM anti-inflammatory explant	4.04 (0.59 to 27.55)	0.154
Post-operative serum drops: Required Referent: not required	5.65 (0.87 to 36.61)	0.069
Post-op therapeutic contact lens: Required Referent: not required	6.91 (1.80 to 26.52)	0.005

AM, amniotic membrane; BM, basement membrane.

*Odds ratios of <1.0 suggest protective effect against failure.

Table 5 Outcome for chemical injury according to severity

Chemical/ Thermal injury grade	Satisfactory outcome n (%)	Intermediate outcome n (%)	Failure n (%)	Total
Grade 1	1 (14.3)	2 (28.6)	4 (57.1)	7
Grade 3	1 (50.0)	1 (50.0)	0	2
Grade 4	3 (33.3)	1 (11.1)	5 (55.6)	9
Total	5	4	9	18

Our analysis indicated that preoperative use of topical steroids appeared to be a factor associated with failure. 74% (65/88) of PED patients were receiving topical steroids prior to AMT. However, reduction of inflammation is necessary to promote healing, and topical unpreserved steroids are useful in these circumstances, providing there are no adverse effects from toxicity. Of the cases with chemical and thermal injury, with or without LSCD, the association of topical steroids with failure may have indicated a more severe injury, and consequently a poorer prognosis.

The most common operative techniques for PED were use of AM as an overlay patch BM side up, over the cornea (76/233, 33%) and a second piece of membrane sutured BM side up as a graft, within the confines of the defect (44/233, 19%). Suturing within the confines of the defect showed a trend to protection against failure, although the result was not statistically significant. AM was used with the stromal side up in 9% (7/88) of PED cases. This use of AM as a "biological bandage" is believed to trap inflammatory cells while epithelialisation is occurring beneath the membrane.

Dua has described overlapping the edges of an overlay patch of amnion with the edge of recessed peritomised conjunctiva, in an attempt to ensure that centripetally migrating epithelium from the conjunctiva will grow on the overlay amnion and not on the corneal surface.² This technique was used in 4.6% (4/88) of cases.

Lamellar or penetrating grafts were performed concomitantly with AM surgery for PEDs in 7% (6/88) of patients. AM as an overlay patch may be useful in promoting postoperative epithelialisation of corneal grafts, particularly in neurotrophic corneas.

Limbal stem cell deficiency

AM transplantation alone, following removal of corneal pannus, has been reported to be successful for treatment of patients with partial limbal stem cell deficiency.¹¹ In this study, clinical demonstration of a corneal phenotype occurred in 57.1% (4/7) of cases, of which half had partial LSCD. It may be argued that cases with mild LSCD could have healed successfully following pannus removal, with or without an AM transplant.

Conjunctival Reconstruction

AM appeared to be successful in repair of conjunctival defects, although 48% (11/23) had an intermediate result with residually inflamed or scarred conjunctiva. Previous work has shown that AM grafting following primary and recurrent pterygium excision can be associated with unacceptably high recurrence rates.¹⁶⁻¹⁸ A recent prospective randomised study showed a pterygium recurrence rate of 40.9% with AM grafts compared with 4.76% for conjunctival autografts.¹⁸ It may in addition be less successful than other techniques such as the use of buccal mucous membrane.³² AM is probably most useful as an adjunct to a conjunctival autograft when a large conjunctival defect has to be covered and there is inadequate

conjunctiva for an autograft, as in primary double head pterygia, and also for large recurrent pterygia. In the latter cases, concomitant use of intraoperative antifibrotic agents such as mitomycin C may also reduce the risk of another recurrence.

Uncontrolled case series indicate favourable results of AMT following excision of large ocular surface neoplasias,¹⁴⁻¹⁵ although symblepharon formation and partial LSCD may still result. How this compares with no coverage of the resultant defect, conjunctival grafts³³ or mucous membrane grafts, is unknown. An advantage in using AM in this situation is elimination of donor site morbidity.

AMT for conjunctival fornix reconstruction and excision of conjunctival cicatrix, combined with intraoperative mitomycin C, has been reported to be useful even after failed mucous membrane grafting.²¹ Mitomycin C was not used in this current study which may have adversely influenced the outcome. Another series reported a 30% rate of cicatrization following treatment of symblepharon associated with burns and Stevens Johnson syndrome, commenting that the severity of dry eye influenced the success of surgery.²⁰

Bullous keratopathy

In eyes with poor visual potential, which are not suitable for penetrating keratoplasty, AM transplants have been reported to result in pain relief in 88% by 12–45 months. The results in this study were not promising, with resolution of pain in only 50% (9/18) by 3 months postoperatively. The difference in follow-up duration time may be partly responsible for these differing success rates but it is unlikely that the results would have improved with a more prolonged follow-up. The success of AM transplants in comparison with conjunctival flaps, phototherapeutic keratectomy, therapeutic contact lenses and anterior stromal puncture in these eyes has not been investigated.

Chemical injury

In this study, AMT appeared to be successful in 27.8% (5/18) of patients with chemical injuries, but failed in 50% (9/18). Both grade 4 and grade 1 injuries were associated with 56–57% failure. Whilst the results for grade 4 injuries are consistent with previous reports, the results for grade 1 injuries are contrary to those reported by other workers.²²⁻²³ A recent randomised controlled trial has shown no difference in the rate of healing, the development of vascularisation and symblepharon formation in patients with both moderate and severe chemical injuries, although comfort was significantly improved in patients with moderate burns having AM grafts.²⁴

When interpreting the outcomes in this study, a major limitation is the 54% (126/233) valid three month follow-up returns, which could have introduced bias in the unlikely event of differential reporting of cases with success or failure. The criteria specified for a 'Satisfactory' outcome, for example in CHEM and BK, may also be considered to be more stringent than criteria used in other reports, resulting in lower proportions of success. The short follow-up duration of only three months may also have influenced the rates of success and failure. With longer follow-up, the success rates for healing of persistent defects, BK and chemical injuries might have been higher although we feel the converse is likely.

This study evaluated the indications and outcomes of a new therapy, when it first became widely available in the UK, through the involvement of a user group. Before the provision of AM by the NLTB there were, to our knowledge, only two surgeons using this technique in the UK. When a new treatment modality is first introduced, it is frequently considered for cases that have been resistant to conventional treatment, so that patients selected for the new treatment are of

poorer risk. After this initial introductory period, patient selection may not show this bias and the results might be different.

The aim of this paper was to evaluate the indications for the use, techniques and outcomes of AMT when it became easily available to a large group of surgeons specialising in corneal and external disease (the AMTUG). It is likely that some surgeons may not have been as expert at selecting and treating this complex group of diseases as the authors of previous case series, or of those reporting the few clinical trials of AMT, but the results we describe are what AMT was used for, how it was used and describe the outcomes for a subset of the patients. As such the evaluation of AMT using this user group model provides data that cannot be obtained from case series or clinical trials, and may be more representative of outcomes generally available to patients.

This user group model may be of value for other new technologies, and is practical where the supply is limited and the user group is small. Even with a user group as small as AMTUG, obtaining complete and valid data is challenging and might have been improved by including this as part of an annual audit by each department.

Whilst AMT is a welcome and useful addition to the range of therapies available for ocular surface problems, the quality of evidence for its use would be improved by further controlled clinical trials. Evaluation of its benefit compared to current alternatives in BK and PEDs apart from neurotrophic ulcers would be ideal. In addition, all allograft transplants carry risks to the recipient and the decision to use such grafts must be based on risk assessments taking into account the possible, albeit remote, likelihood of transmitted disease. Adherence to appropriate standards such as the requirements of the Directive 2004/23/EC for tissues and cells³⁴ will minimise those risks.

Appendices are available on the BJO website <http://bj.o.bmj.com/supplemental>

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