earlier suggestions that the observed clearing was the result of two processes. In his phraseology: (a) scleral tissue is replaced by collagenous fibres from the recipient cornea; and (b) scleral fibres assume the properties of those in the cornea.

In the case described here, the challenge was to repair a peripheral defect in the cornea with minimal disturbance to axial tissue, and thus vision.

Fibrils within the sclera are of more irregular diameter and arrangement than those in corneal stroma and, as a result, sclera is of greater tensile strength.^{4,7} We chose to use sclera rather than corneal tissue to repair the defect as, because of its higher tensile strength, a smaller and thinner sliver of tissue could be used. This made it possible to avoid any disturbance to the contour of the central cornea and gave a rapid stable improvement in vision.

Another advantage of autologous scleral grafting is the ease of availability of tissue. This is particularly relevant in emergency procedures where there may not have been sufficient warning to obtain corneal donor material. There is also, of course, no risk of rejection.

We have since used autologous scleral grafting in two other cases of corneal perforation and suggest that it is a useful and valuable technique, which has been largely overlooked since it was first described in 1948.

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Corneal transplant rejection following influenza vaccination

Corneal transplant is the most commonly performed transplant surgery in the United Kingdom. From 1995 to 2005, over 23 000 corneal transplants have been performed in the United Kingdom alone, with 2378 performed from 2004 to 2005.¹ This equates to a rate of 40.3 per million population per year in the United Kingdom.¹ The reported rates of corneal transplant rejection vary from 8% to 37%.² We report on three cases (two patients) of corneal transplant rejection following influenza vaccination. General practitioners, ophthalmologists, and their relevant patients should be aware of this small but potentially

sight threatening complication. Appropriate patients should be informed and warned of the symptoms of corneal transplant rejection before consenting to having the influenza vaccination. If diagnosed early, corneal transplant rejection is potentially reversible, albeit with endothelial cell loss.

A 67 year old woman presented to the eye department with a 5 day history of a red, uncomfortable left eye associated with blurring of her vision. She had undergone an uncomplicated corneal transplant 8 months before this consultation. Ocular examination revealed classic signs of corneal transplant rejection in the epithelium (Krachmer spots), stroma (oedema and swelling) and endothelium (keratic precipitates) (fig 1). On further questioning it was revealed that she was given the influenza vaccination (Sanofi-Pasteur MSD, UK) 2 weeks before the onset of her symptoms. This patient was started on hourly drops of prednisolone acetate 1% to treat her acute corneal transplant rejection episode. She made a good recovery and the transplant settled satisfactorily. The prednisolone acetate 1% was tapered to one drop per day. Four months after the influenza vaccination the patient is symptom free and the corneal transplant remains clear and devoid of signs of active rejection.

Another 67 year old woman presented to the eye casualty department with a 3 week history of a red, painful right eye associated with blurring of her vision. She had undergone an uncomplicated, routine corneal transplant 7 months before this assessment. The patient had signs of corneal transplant endothelial rejection, including inflammation in the anterior chamber, keratic precipitates, and a swollen, oedematous cornea. She had had an influenza vaccination (Sanofi-Pasteur MSD, UK) 3 weeks before developing these

symptoms. She was successfully treated with a tapering dose of prednisolone acetate 1% and the rejection resolved.

The same patient presented to the eye department 1 year later with a 1 week history of a painful, red right eye with blurred vision. Slit lamp examination revealed another acute episode of corneal transplant endothelial rejection with a swollen, oedematous cornea and keratic precipitates. This patient had undergone her yearly influenza vaccination 4 weeks before developing the symptoms of rejection. After intensive steroid drop therapy the patient's symptoms resolved and the cornea cleared, and the rejection episode was successfully treated.

Comment

The exact immunological mechanism of corneal graft rejection is not fully understood. Numerous animal and experimental models have been created to further understand the mechanism. The cornea is a site of immune privilege. Immune privilege is due, in part, to the fact that the cornea is devoid of blood and lymph vessels in the host bed and the lack of MHC class II antigen presenting cells in the donor cornea³ and therefore systemic immunosuppression is not prescribed routinely in patients undergoing routine, low risk corneal transplantation. Therefore, unlike other solid organ transplant recipients, corneal transplant patients do not require immunosuppression and therefore can mount a normal host response to antigen. There are no reported cases of transplant rejection in liver, lung, and kidney recipients following the influenza vaccination.⁴ There are however conflicting reports on whether the influenza vaccination may or may not cause low level rejection in heart transplant patients.⁴ The Department of Health recommends that all immunosuppressed patients be vaccinated against influenza; this includes patients on systemic immunosuppression.⁵

In 1996, Solomon *et al* reported a case of bilateral corneal transplant rejection following influenza vaccination⁶ (table 1). Steineman *et al* reported on five patients with corneal transplant rejection associated temporally with hepatitis B, tetanus booster, and influenza vaccinations⁷ (table 1). To our knowledge there are no further reports of corneal transplant rejection associated with the influenza vaccination.

General practitioners and ophthalmologists should be aware of this small but potentially sight threatening complication following flu vaccination. We do not advocate that the influenza vaccination not be administered to these patients, but patients should be told of the possible link between the influenza

Figure 1 Slit lamp photograph showing subepithelial infiltrates (small arrows) and a keratic precipitate (large arrow) on the endothelium. These are both classic signs of corneal graft rejection.

Table 1 Comparison of the literature of corneal transplant rejection following influenza vaccination

Study	Year	Patient age (years)	Time from CT to CTR	Time from IV to CTR	CTR resolved
Wertheim <i>et al</i>	2006	67	8 months	2 weeks	Yes
		67*	7 months	3 weeks	Yes
		68*	18 months	4 weeks	Yes
Solomon <i>et al</i> ⁶	1996	80	11 years	6 weeks	Yes
Steinemann <i>et al</i> ⁷	1988	73	3 months	3 weeks	Yes
		69	4 months	3 weeks	No
		72	6 months	8 weeks	Yes

CT, corneal transplant; IV, influenza vaccination; CTR, corneal transplant rejection.

*Same patient with two separate episodes of corneal transplant rejection.

vaccination and corneal transplant rejection. If patients have symptoms of corneal transplant rejection, including blurred vision, injected eye and discomfort, they should contact their general practitioner or ophthalmologist immediately. Rejection can take place up to 2 months after influenza vaccination and is potentially reversible. However each rejection episode leads to the inexorable loss of endothelial cells and potentially irreversible graft failure. Owing to the increased publicity of potential influenza pandemics and the increased uptake of vaccination, we think that it is important that this causal relation, between influenza vaccination and corneal transplant rejection, be recognised and publicised.

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MAILBOX

Eyelid basal cell carcinoma

We read with interest the paper by Hamada *et al.*¹ which draws a number of conclusions from a 5 year follow up study of 69 periocular basal cell carcinomas (BCCs) treated by conventional surgery and, in particular, suggests that there is no place for Mohs micrographic surgery (MMS) in patients with periocular BCCs. MMS is the serial saucerisation excision with mapped horizontal tissue sections examining 100% of the surgical margins to produce histological evidence of tumour negative margins. Unfortunately, the data included in the paper are incomplete and if such conclusions are to be considered, then further clarification is required.

Risk of BCC recurrence relates directly to the nature of the tumours treated.² The

principal risk factors for recurrence include previous treatment, large tumour size, and an infiltrative or micronodular histological growth pattern. No information is given on the first two factors and the histological subtype was non-specified in approximately 45% of cases. We calculate from the data provided that the authors experienced a 19% 5 year recurrence rate in patients with a histologically infiltrative BCC.

If most of the “non-specified” tumours in Hamada’s series were small nodular tumours, as the paper implies, then Hamada’s series also differs significantly from other larger series in that it represents a group of patients with an inherently better prognosis. Other comments hint at this, in that 76% of BCCs were on the lower eyelid and 72% were amenable to direct closure. If the majority of the tumours in this series were not in a high risk group then only one recurrence would be anticipated. In contrast, the Australian Mohs’ database series³ reported on a much higher incidence of high risk tumours (50% were infiltrative, morphoeic, basosquamous, or superficial), of which only 54% were on the lower eyelid while 41% affected the medial canthus, a site with a proved higher risk of recurrence. Despite this, they reported a 0% recurrence rate for primary BCCs of all histological subtypes treated by MMS surgery.

Hamada *et al* also conclude that 4 mm margins are justified for well defined nodular tumours, on the basis of the 5 year recurrence rates and the fact that most eyelids can still be directly repaired after such excisions. It is of interest, however, that 16% of the patients reported had incomplete tumour excision at the first attempt, although we do not know what margins were used for this group. As conventional pathological sectioning examines less than 1% of the margins,⁴ it is likely that the actual incomplete excision rate was higher.

Hamada *et al* argue that MMS is not necessary for periocular tumours on the basis that it is difficult to obtain true MMS sections. Unless either periosteum or anterior orbital septum are breached by the tumour, then there is no evidence for the former statement. What about cost benefit? MMS histology costs are greater than routine sections. However, when the other advantages of MMS are taken into account MMS is cost effective in comparison with traditional surgical excision.⁵

The current best evidence shows that recurrence rates are lower with MMS than with any other technique, with MMS for recurrent or high risk tumours showing the greatest advantage over conventional surgery. Furthermore, Hamada *et al* acknowledge that the tissue sparing quality of MMS is an important issue in that 36% of patients will develop a second BCC within 5 years.

Although we believe that MMS is the treatment of choice for optimal cure rates in periocular BCC, we would agree with Hamada *et al* that it is currently impractical for all tumours because of the patchy availability of the service in the United Kingdom. However we believe the current evidence shows that MMS remains the optimal treatment for all high risk tumours based on treatment status, site, size, and histological subgroup and do not feel that the data presented warrant a different conclusion.

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Authors’ reply

We thank Barnes *et al* for their interest in our study and for affording us the opportunity to correct some misinterpretations that others may also have made regarding our paper.¹

We agree entirely that histological examination of the complete excision surface as suggested by Mohs would be the ideal one should aim at and that it would be superior to conventional bread loaf histological sectioning. We dispute that this is realistically possible in inhomogeneous and exceedingly mobile eyelid tissues unless they are fixed before excision as in the chemosurgery that Mohs originally described.

Trying to cut a complete 2 mm thick saucer of tissue through fresh skin, orbicularis, tarsal plate, orbital septum, and fat and then transferring it without distorting the relative tissue orientation is a challenge that few are equal to. It might have been helpful if Barnes *et al* had shared their practical experience of the technique with us in their letter.

That the risk of basal cell carcinoma (BCC) recurrence relates to the tumour type is not in dispute and is indeed borne out in our results. But it is helpful of Barnes *et al* to remind other readers of this fact. Histological subtype was not specified in the greater portion of our series as our histopathologists only pass comment when BCCs are infiltrative or unusual in other respects. We apologise for not stating this explicitly as it has clearly led to some misunderstanding.

However, there is no justification for Barnes *et al*’s assumption that the “non-specified” tumours were small because 72% were managed by direct closure. We have clearly failed to get over a most important point. Direct closure under tension is not only possible in much larger lid defects than conventionally taught but also gives far superior functional and cosmetic results. As such, we urge others to use this method of repair more widely.

That 76% of our tumours occurred on the lower lid should not come as a surprise to anyone as it is a well recognised fact. It does not suggest that our series is in any way biased.

That our series differs from the selected series in the Australian Mohs database is self evident. We described our experience with an