Peritoneal autografts in conjunctival replacement

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The successful treatment of severe symblepharon and conjunctival scarring still eludes ophthalmologists today as it did the ancient Greeks when Heracleides first described the operation of dividing limiting adhesions with subsequent mobilization of the lids. This is still current practice, but in severe cases a conjunctival replacement graft is required. Buccal mucous membrane is most commonly used, but a variety of different tissues have been tried in the past, none of which has proved very satisfactory either because it did not function adequately or was poor cosmetically, or because there was insufficient membrane available.

In 1873 Wolfe first transplanted rabbit conjunctiva to a human, and presumably his xenograft failed. Taylor (1876a, b) successfully treated symblepharon by reconstructing a fornix with a pedicled skin flap; but any lining by skin is unsatisfactory as hairs are always present on all skin except the palms of the hands and soles of the feet, and if the eye is *in situ* these may cause acute discomfort and corneal ulceration. The skin itself also irritates the eye by desquamation (Mustardé, 1966).

Van Millingen (1887) gave the first successful account in English of lining by oral mucous membrane which he used to increase the conjunctival surface and cure the trichiasis of entropion. Denig (1911, 1912, 1918, 1920) published a series of papers encouraging ophthalmologists to use buccal mucous membrane grafts in the replacement of scarred conjunctiva and in the early treatment of burns, and indeed buccal mucous membrane is most commonly used today.

Earlier workers (Bock, 1884; Stellwag von Carion, 1889) had employed oral mucous membrane and the latter subsequently tried transplants from vaginal mucous membrane instead of oral mucous membrane in the hope that this would not shrink so much as the thin oral mucosa, but with disappointing results.

Wiener (1926) was the first worker to use nasal mucosa from the middle turbinate, and nearly 50 years later Stallard (1973) was successful with the lining of the antrum removed in one piece through a Caldwell-Luc approach.

Clay and Baird (1963) reported satisfactory results with transplants from prepuce and labia minora,

and Mackenzie (1946) used rectal mucosa. Cadaver conjunctiva was first used by Rosenweig (1938) and Straub (1969) reported satisfactory results with this method. The first worker to use fetal membranes appears to have been De Rötth (1940) and this material was subsequently employed by Sorsby and Symons (1946). De Rötth claimed that amniotic membrane retained its embryonic ability to metamorphose completely to adult conjunctiva and therefore ought to be the best conjunctival substitute. Sorsby and Symons (1946) similarly suggested that the amniotic membrane graft acted 'biologically rather than mechanically'. Working with fetal membranes, however, is extremely difficult.

The use of peritoneum was first reported in 1940 by Nachminović who transplanted a strip of peritoneum 2.5 cm × 1 cm, to replace trachomatous scarring and pannus of the upper limbus. Subsequently Allen (1953) reported success with autogenous peritoneal grafts in two cases of contracted sockets, and in two cases after superficial keratectomies and extensive removal of bulbar conjunctiva. He concluded that peritoneum was a satisfactory substitute for conjunctiva. Malhotra (1957) also reported successes, but he used stored peritoneum removed from hernial sacs and tunica vaginalis from hydrocoele sacs. Similarly Erbakan (1960) used peritoneum, taken from hernias, to reconstruct contracted sockets. Both Malhotra (1957) and Erbakan (1960) appear to have used heterografts, but Nath, Shukla, Nema, and Kumar (1964) employed auto-peritoneal grafts of greater omentum as Allen (1953) had done with considerable success; they completely replaced the conjunctival cul-de-sac in one patient who also had a parotid duct transplantation and obtained a successful result with a 12-year follow-up (Nath, 1973).

Clinically buccal mucous membrane is the tissue most commonly used at the present time for conjunctival replacement, but it is not ideal as it tends to be bulky and is not a very good colour match, and there is only a limited amount available at any one time. In theory a partial thickness graft of mucous membrane can be taken repeatedly from the same buccal mucosa after it has regenerated, but in practice there is often extensive scarring in the mouth if successive grafts have been removed. For this reason peritoneum taken from the greater omentum has been

recommended where more extensive conjunctival replacement is required in one or both eyes (Stallard, 1958). However, despite the successes published by Allen (1953), Malhotra (1957), Erbakan (1960), and Nath and others (1964), other workers have had no success with peritoneum (Fox, 1963; Alberth, 1968). The purpose of this study was, therefore, to establish experimentally in animals whether peritoneum could function as a conjunctival substitute, and if so, to determine histologically the fate of the graft.

A series of 28 rabbits underwent conjunctival replacement with peritoneal autografts. They were subsequently killed at various intervals and the tissues examined histologically.

Technique

Dutch rabbits weighing between 1.5 and 2.5 kg were anaesthetized with intravenous thiopentone *via* an ear vein and cannula. The abdomen was shaved and opened *via* a mid-line incision. Parietal peritoneum, with its associated transversalis fascia, was separated from the abdominal wall by opening up a plane of cleavage with saline injected through a lacrimal cannula. The graft was then excised, cleared of all adherent muscle and fat, and temporarily sutured to its fellow from the other half of the abdominal wall. Greater omentum was not used as there is an insufficient amount of this material in a rabbit. The abdomen was then closed with continuous catgut to the muscles and interrupted black silk sutures to the skin. Lid sutures were placed in the right upper and lower eyelids and the conjunctiva was elevated from the globe, fornices, and upper palpebral regions with a subconjunctival injection of 2 per cent lignocaine with adrenaline. The conjunctiva and underlying Tenon's capsule were then excised from the lid margins with the nictitating membrane, leaving a small area of adherent palpebral conjunctiva which could not be stripped off the upper and lower tarsal plates. During the operation the partially excised

conjunctiva protected the corneal epithelium, and was excised from the limbus at the last stage. The autoperitoneal graft was then laid on the globe, care being taken that the previously intra-abdominal surface was lining the newly constructed conjunctival sac. It was sutured to the limbus with interrupted virgin silk sutures and to the cut tarsal conjunctiva at the lid margin with a continuous nylon suture. The fornices were reconstructed with deep interrupted nylon sutures which were removed with the continuous suture at 7 to 10 days post-operatively. The rabbits were all given systemic and topical antibiotics initially and later local steroids were used selectively.

Results

The grafted rabbits were killed at various intervals and histological sections cut and stained. These showed that the initial change was a proliferation of the remaining conjunctival epithelium at both the tarsal and limbal junctions, and a flattening of the surface mesothelial cells of the graft. The proliferating conjunctival epithelium then migrated over the surface of the graft replacing it with a single layer of flattened epithelial cells (Figs 1-4). These cells then multiplied to produce an epithelium three to four cells thick, which contained goblet cells (Fig. 5). The subepithelial tissue of the graft derived from the integrally associated transversalis fascia was initially invaded by typical granulation tissue with its capillaries and fibroblasts, and subsequently underwent replacement fibrosis.

The original mesothelial surface of the peritoneal graft did not contain goblet cells and therefore their presence in the re-formed conjunctiva indicates that they must either have been derived from surviving conjunctiva or have been formed by metaplasia. When all the original conjunctiva was removed or destroyed, the peritoneal graft was replaced by a mass of fibrous tissue and no true surface epithelium

FIG. 1 Normal rabbit conjunctiva. Periodic acid-Schiff and haematoxylin (PASH) $\times 344$

FIG. 2 *Rabbit conjunctiva, one week postoperative. Host/graft junction showing proliferating host conjunctiva spreading over flattened mesothelial cells of graft. PASH $\times 144$*

FIG. 3 *Rabbit conjunctiva, 12 days postoperative. Higher power view of host/graft junction showing subepithelial tissues now invaded by granulation tissue. PASH $\times 387$*

FIG. 4 Rabbit conjunctiva, 5 weeks postoperative. Shows single layer of flattened conjunctival cells covering graft. PASH $\times 387$

FIG. 5 Rabbit conjunctiva, 2 months postoperative. Shows that conjunctiva has now proliferated and includes goblet cells (arrowed). PASH $\times 800$

FIG. 6 Rabbit conjunctiva, 7 months postoperative. Shows almost normal appearance of graft. PASH $\times 621$

or goblet cells were formed. The peritoneal graft did not, therefore, retain its own identity or undergo metaplasia to form a new conjunctiva, but only functioned as a 'scaffold graft' being replaced by healthy conjunctival elements in a process of 'creeping substitution'. This process, however, was very effective and after 6 months the conjunctiva appeared almost normal, both clinically and histologically (Fig. 6).

Discussion

Duke-Elder (1965) stated that mucous membrane derived from other localities such as the mouth or vagina when transferred to a raw area in the conjunctival sac readily adapted to its new environment and almost invariably 'took'. Histological examination showed that it assumed all the characteristics of the ocular conjunctiva, even participating typically in its diseases. Stepanok, Tagibekov, and Golovshenko (1969) confirmed that lip mucosa preserved its normal histological structure, including salivary glands, when transplanted in plastic operations for orbital reconstruction. Peritoneum, however, is not a mucous membrane, but only a thin serous mesothelium and this is probably the reason why it only acts as a scaffold graft.

It is also possible that the results of experiments in rabbits are not applicable to man. Ballen (1963), however, grafted buccal mucosa into rabbit eyes and histologically the grafts appeared to take. If buccal mucosa grafts behave similarly in rabbit and man, it is reasonable to assume that peritoneal grafts will behave in the same manner. The only reference in the literature to the use of rabbit peritoneum appears to be that described by Brown (1941) who utilized it in lime burns as a 'protective bandage' or temporary onlay and not as a graft.

It is perfectly feasible that all the previously reported successes with peritoneum have depended upon the presence of sufficient surviving healthy conjunctival elements to use the peritoneal graft as a scaffold.

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This would equally well account for the failure of other workers if in their cases there was insufficient remaining healthy conjunctiva or none.

Conclusions

Peritoneal grafts function as a scaffold being replaced with conjunctiva by creeping substitution. It is therefore only possible to consider using peritoneum as a conjunctival replacement and in orbital reconstruction work providing there are sufficient healthy conjunctival elements surviving which remain capable of proliferation. In such cases Merz and Czerwińska (1969) have shown that an inert material like silicone rubber will form a temporary scaffold which allows proliferating conjunctiva to reconstitute a surface epithelium. It would therefore appear that, if peritoneum acts only as a scaffold, the indications for exposing a patient to the risks of obtaining it autogenously are very rare. The vast majority of patients requiring a conjunctival graft should have a mucous membrane graft which will survive in its own right and does not need to be replaced by healthy proliferating host conjunctiva which in fact is likely to be deficient in these patients.

Summary

Twenty-eight rabbits underwent conjunctival replacement with peritoneal autografts. The grafted peritoneum acted as a scaffold for the remaining healthy conjunctiva which gradually replaced the grafted peritoneum. Peritoneum is not an effective conjunctival substitute as it does not survive in its own right.

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