PERIPHERAL NERVE REPAIR IN HUMANS USING MUSCLE AUTOGRAPHS
A NEW TECHNIQUE

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Coaxial autografts of skeletal muscle which had been frozen then thawed were used to repair injured digital nerves in eight patients. Assessment from three to 11 months after operation showed recovery to MRC sensory category S3+ in all but one patient, an excellent level of recovery. We conclude that bespoke muscle grafts treated and used in this way may offer significant advantages over conventional nerve grafts or cable grafts especially where large peripheral nerves are involved.

In 1954 the Medical Research Council Report on Peripheral Nerve Injuries reviewed mechanisms of regeneration and analysed results of repair of injuries to peripheral nerves (Seddon 1954). Since then, although technical improvements have resulted from microsurgery there have been few large controlled trials, and the relative merits of immediate and delayed repair, or of epineural as against fascicular repair are still undecided. Fascicular repair remains popular with clinicians despite the evidence of Morris, Hudson and Weddell (1972), and of Mackinnon, Hudson and Hunter (1985), which cast doubt upon its basic merit.

Thomas and Jones (1967) have suggested that the perineurial cells have a role in establishing the correct environment for nerve function; these cells may be important in defining the level of fasciculation of the regenerating nerve pathway, but this process is ill-understood. Achieving a perfect replica of the original “wiring” seems highly improbable since regenerating axons would need to find the correct tube and the intraneural plexus is disturbed when there is a traumatic gap. The goal at present must be to provide the regenerating fibres with a matrix of “endoneurial tubes” orientated so that maximum numbers may reach the target organs in minimum time (Sanders 1954).

It is now known that regenerating nerve fibres can provide themselves with Schwann cell basement membrane and with perineurial cell and basement membrane tubes, but the provision of appropriately orientated empty tubes in the crucial, early stages of regeneration, ensures that an optimal number of fibres reach their targets quickly (Davies et al. 1987).

Where the nerve injury leaves a gap which cannot be bridged by direct suture, the outlook is considerably worse. If the damaged nerve is of small diameter the gap may sometimes be usefully bridged by a nerve autograft. A typical graft is a cutaneous nerve such as the sural nerve; but this contains only small diameter fibres. The endoneurial tubes are then too small to accommodate the fibres which it is most desirable to have regenerate, namely, motor and the larger sensory fibres.

When the damaged nerve is a large one such as the median, sacrifice of a nerve of appropriate diameter is very rarely justified (Seddon 1954). Repair is then usually by a “cable graft” made from several strands of cutaneous nerve. The same problem of tube size arises and is worse when large fibres form a high and important percentage of those in the nerve trunk. In addition, the gaps between the strands of the cable fill rapidly with connective tissue which may obstruct useful pathways (Gutmann and Sanders 1943). Glasby et al. (1986a), considered the possibility of using non-neural autografts for nerve repair. Skeletal muscles with fibres in a parallel array have an orientated matrix of basement membrane tubes, which is, anatomically and probably chemically, similar to that of peripheral nerve (Ide et al. 1983; Ide 1984; Tohyama and Ide 1984; Tohyama 1985). The

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muscle-derived basement membrane tubes are all large enough to accommodate the largest nerve fibres.

Sanes, Marshall and McMahan (1978) had shown that peripheral nerve fibres can grow into skeletal muscle when it degenerates; it seemed that if regenerating axons could grow through a muscle graft and out again to re-enter the distal end of a peripheral nerve, then muscle could provide clinically acceptable and abundant graft material. This was shown to be the case in the rat and monkey for frozen and thawed grafts by Glasby et al. (1986b,d), and confirmed in the rabbit by Fawcett and Keynes (1986), though these authors used chemical means to degenerate their grafts. In primates, Glasby et al. (1986d) had repaired 3 cm gaps in the ulnar and radial nerves with muscle grafts and gained effective recovery. For similar diameters of graft, muscle grafts performed as well as conventional whole nerve grafts (Glasby et al. 1986c).

In all of Glasby's work the sarcoplasm contained within the basement membrane tubes had been disrupted by freezing in liquid nitrogen and then thawing in distilled water. Davies et al. (1987) showed that this treatment, combined with coaxial interposition of the graft, optimised the growth rate of the fibres across the graft and into the distal nerve. Simply leaving a gap in the transected sciatic nerve of the rat resulted, as might be expected, in the formation of a proximal neuroma and a distal glialia (Young 1942; Blackwood and Holmes 1954). In the rat, (Gschmeissner et al. 1987) and in primates (Gattuso et al. 1988), the technique of repair with muscle grafts was shown to allow new motor endplates to be established by the regenerated axons in their target muscles. Clinical, electrophysiological, histological and histochemical examination demonstrated functional recovery.

Parallel arrays of autogenous skeletal muscle fibres are readily available, sometimes through the same incision as that used for the nerve repair. The freeze-thawing process takes only a few minutes and the resulting grafts may be tailored to any size. Such a graft, if it performs at least as well as a conventional nerve graft, offers a useful alternative and is probably superior to a cable graft, since tube size is greater and there are no interstices.

Our animal experiments had shown this to be the case and we now report eight cases of repair of digital nerves by this technique.

**METHODS AND MATERIALS**

Over an 11-month period, nine patients, aged 15 to 61 years, consented to repair of a digital nerve with a freeze-thawed muscle autograft. One was lost to follow-up; in the eight remaining cases gaps of 15 to 25 mm were bridged. The experimental nature of the trial and its importance for the repair of large nerves was explained to each patient and signed consent forms were obtained. All operations were performed by the same surgeon (RWN).

**Technique of operation.** Autologous graft material is obtained at the time of nerve repair by excising a rectangular block of muscle from the inferior border of pectoralis major in the anterior axillary fold. This site was chosen since the muscle fibres are in parallel bundles and a remote donor site would minimise damage and potential morbidity at the site of the repair.

The block of muscle is frozen in liquid nitrogen until thermal equilibrium is obtained and then thawed in sterile distilled water. This takes about five minutes, during which time the recipient site is prepared. The graft is trimmed to the appropriate size to bridge the gap, keeping its long axis aligned. The definitive graft is, then, a rectangular block as long as the gap in the nerve and about 2 mm wider in each plane than the diameter of the nerve. This leaves ample cross-sectional area for anchoring sutures and for the free passage of axons.

The prepared graft is interposed coaxially between the proximal and distal ends of the severed nerve and, under an operating microscope, the graft is sutured into place using 9–0 or 10–0 polypropylene or polyamide interrupted stitches. These traverse the epineurium of the nerve and only the extreme periphery of the muscle graft (Glasby et al. 1986a,b,c,d). After the operation, early mobilisation of the hand is encouraged, rather than the more traditional splinting for the first 10 to 21 days.

**Assessment.** Methods for assessment of peripheral nerve repair have been extensively reviewed by Bowden and Sholl (1954), Seddon (1954, 1975) and Zachary (1954). The MRC grading of sensory recovery was used (Table 1). All testing was performed by one experienced observer (REMB), in a quiet, well illuminated, warm room. Light tactile sensation and localisation were tested using von Frey hairs graded 1 to 7.

In testing localisation a von Frey hair of appropriate calibre was applied with the patients' eyes closed. The patient was then asked to open his eyes and localise the point of contact with an orange-stick. Particular atten-

**Table 1. MRC grading of sensory recovery in the autonomous area of a nerve (Zachary 1954)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>S 0</td>
<td>Absence of any sensory recovery</td>
</tr>
<tr>
<td>S 1</td>
<td>Recovery of deep cutaneous pain sensibility</td>
</tr>
<tr>
<td>S 2</td>
<td>Return of some superficial pain and tactile sensibility</td>
</tr>
<tr>
<td>S 2+</td>
<td>Recovery of touch and pain sensibility throughout the autonomous zone but with persistent over-reaction</td>
</tr>
<tr>
<td>S 3</td>
<td>Return of superficial pain and tactile sensibility throughout the autonomous zone with disappearance of over-reaction</td>
</tr>
<tr>
<td>S 3+</td>
<td>As S 3 but with good localisation and some return of two-point discrimination</td>
</tr>
<tr>
<td>S 4</td>
<td>Return of sensibility as in S 3, with recovery of two-point discrimination</td>
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</tbody>
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tion was given to this assessment of localisation, since this gives an indication of both density of innervation and the presence or absence of misdirection of regenerated axons. Two-point discrimination was tested with a fine caliper and 5 g and 10 g loaded pins were used to test for pressure/pain.

RESULTS

Table II shows the results obtained in eight patients. On the MRC sensory recovery grades, all but one of the eight patients had attained Grade S3+ by the time they were assessed at three to 11 months. The one exception had particular difficulty with two-point discrimination and was equally unreliable in tests on the normal hand.

Our results showed no obvious difference between achieved by other means; accordingly we used simple methods of assessment appropriate to a busy out-patient department. One of the authors of the original MRC report performed the sensory testing. We tried to establish that muscle grafts gave results which were at least comparable to conventional methods of repair. If this was the case, then the ease of acquisition and the lack of limitation in graft size or tube size would make bespoke muscle grafting a very attractive technique. Our results have supported this contention.

The high degree of localisation obtained makes it unlikely that the results were the consequence of overlap, since localisation was not referred to the possible donor nerve. Recovery by overlap takes place in two stages, the first of minor importance only (Bowden 1954; Seddon 1954). More extensive overlap may occur in some areas.

<table>
<thead>
<tr>
<th>Case number</th>
<th>Age in years</th>
<th>Sex</th>
<th>Delay before graft</th>
<th>Interval before assessment (months)</th>
<th>Grades of von Frey hair detected</th>
<th>Localisation</th>
<th>Two-point discrimination (mm)</th>
<th>Pin prick detection 5 g and 10 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42</td>
<td>M</td>
<td>None</td>
<td>9</td>
<td>7 to 2</td>
<td>Good</td>
<td>4</td>
<td>14 Normal</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>M</td>
<td>None</td>
<td>3</td>
<td>7 to 5</td>
<td>Good</td>
<td>5.5</td>
<td>19 Normal</td>
</tr>
<tr>
<td>3</td>
<td>42</td>
<td>F</td>
<td>None</td>
<td>8</td>
<td>7 to 1</td>
<td>Good</td>
<td>4</td>
<td>&lt;6 Normal</td>
</tr>
<tr>
<td>4</td>
<td>61</td>
<td>M</td>
<td>4 months</td>
<td>6</td>
<td>7 to 5</td>
<td>Poor*</td>
<td>4–9</td>
<td>16 Normal</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>M</td>
<td>30 months</td>
<td>9</td>
<td>7 to 1</td>
<td>Excellent</td>
<td>3</td>
<td>&lt;9 Normal</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
<td>M</td>
<td>None</td>
<td>8</td>
<td>7 to 1</td>
<td>Excellent</td>
<td>2</td>
<td>&lt;8 Normal</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>F</td>
<td>None</td>
<td>11</td>
<td>7 to 1</td>
<td>Good</td>
<td>2.5</td>
<td>11 Normal</td>
</tr>
<tr>
<td>8</td>
<td>32</td>
<td>M</td>
<td>None</td>
<td>7</td>
<td>7 to 2</td>
<td>Poor*</td>
<td>Poor</td>
<td>Poor</td>
</tr>
</tbody>
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* Localisation was also poor in the control finger  †D, distal  ‡P, proximal

immediate (hours) or delayed repair (months or years), but numbers are small when compared with Seddon, Medawar and Smith (1943) and Sunderland (1947). A wide range of deformability (von Frey hair) could be discriminated, with the classical gradation of sensory recovery from proximal to distal in those assessed early. Although two-point discrimination was never as good on the grafted as on the normal side, it was present in seven of the eight cases. Localisation was good or excellent in six cases and pin-prick discrimination was excellent in seven cases. Accuracy of localisation was within 1 to 2 mm in all cases, the grading as “good” rather than “excellent” in Table II indicating only a degree of hesitation before accurate localisation of the test stimulus.

DISCUSSION

This pilot study aimed to investigate the ultimate feasibility of using freeze-thawed muscle autografts for the repair of large gaps in mixed peripheral nerves in man. We did not intend to compare the results with those but the sensory stimulus is usually referred to the donor area. In the digits, overlap is always minimal, as witnessed by the persistent loss of sensory function in the relevant area of the ring finger after injuries of ulnar or median nerves which have the classical distribution. In view of this and the very experienced assessor, blocking the other digital nerve was not attempted.

The finding that seven of the eight cases achieved MRC Grade S3+ in the time studied compares very well with other published results, though the extreme diversity of these does not allow for a statistical comparison. Seddon in 1975 reported similar levels of sensory recovery in 52% of digital nerves repaired end-to-end by primary suture and 24% of those repaired by secondary suture. Although he quotes no figures, Seddon also states that autologous nerve grafting is better than secondary suture though less good than primary suture.

The rarity of suitable patients and especially of those who have injured two comparable nerves made it impossible to use internal controls. However, all our patients had sufficient sensory recovery to provide safe,
pain-free hands. It therefore appears that coaxial freeze-thawed skeletal muscle autografts are an acceptable immediate or delayed treatment for digital nerve injuries which require grafts.

Muscle grafts are easily obtained and simply prepared. Being autografts, they are not associated with rejection; in none of the animal experiments was there an inflammatory response to the graft. The need for donor nerve is obviated, and the grafts can be big enough for the largest nerve while containing basement membrane tubes with an internal diameter greater than the largest nerve fibres. The maximal opportunity for regeneration is thus offered to maximal numbers of the pioneering axons.

Our report deals only with a small series of small sensory nerves; but the results have been good enough for us to start repairing large mixed nerves with muscle autografts. This work is in progress and will be reported later.

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