Evaluation of microsurgical internal neurolysis in a primate median nerve model of chronic nerve compression

This study evaluates the effect of internal neurolysis on a chronically compressed primate median nerve as compared with a simple decompression procedure. In 11 adult, cynomolgous monkeys, the median nerve in the carpal tunnel was banded with a silicone tube. After 6 months of nerve compression (mild to moderate compression in our model) in eight monkeys, a microneurosurgical internal neurolysis was carried out on the median nerve of one hand and a simple decompression (removal of band) was carried out on the median nerve of the other hand. Histologic, morphologic, and electrophysiologic evaluation was carried out 6 months later. Six control animals were similarly evaluated after 0, 6, and 12 months of nerve compression. The degree of compression produced was not severe in that it did not cause Wallerian degeneration. Histologic and electrophysiologic improvement was produced in both treatment groups over the two chronically compressed groups (6 and 12 months of compression). While internal neurolysis did not cause intraneural scarring or nerve fiber damage as compared with simple decompression alone, there was no difference noted between the effects of these two treatment methods on the chronically compressed nerve. (J HAND SURG 1988;13A:357-63.)

Susan E. Mackinnon, MD, FRCS(C), FACS and A. Lee Dellon, MD, FACS, Toronto, Ont., Canada and Baltimore, Md.

While peripheral nerve entrapment is a common problem treated by the hand surgeon, the pathophysiology associated with this entity is not completely understood and controversy exists regarding appropriate surgical treatment measures. It has been suggested in both experimental studies and clinical reports that internal neurolysis causes intraneural fibrosis and nerve fiber damage as compared with simple decompression alone. In spite of this controversy, there have been only two experimental studies addressing this problem. This study was designed to evaluate the effect of internal neurolysis of a chronically compressed nerve model of chronic nerve compression.
median nerve in a primate model as compared with treatment by simple decompression.

Material and methods

Using a model for chronic nerve compression in the primate in 11 adult cynomolgus monkeys, with the monkeys under ketamine and acepromazine anesthesia, the median nerve in the carpal tunnel was exposed and banded with a 1 cm length of silicone tubing (internal diameter of 1.98 mm). The silicone tubing was closed with three interrupted No. 8-0 nylon sutures so that the tubing fit snugly about the nerve. The transverse carpal ligament and skin were closed with No. 3-0 nylon suture. One million two hundred thousand units of procaine penicillin was administered intramuscularly during the operation. Similar procedures were carried out in both hands. No splints were used postoperatively. After 6 months of nerve compression in eight animals, an internal neurolysis was carried out on the right median nerve with 3.5 loupe magnification (Figs. 1 and 2). The neurolysis was begun proximal to the region of compression at the level of the epineurium, and an extensive internal neurolysis was carried out with removal of the epineurium and dissection of the median nerve into four to six fascicular groups (Fig. 2). Care was taken not to damage the perineurium. At no time were any windows in the perineurium noted to indicate perineurial damage. In these same eight animals, simple decompression (release of the transverse carpal ligament and removal of the silicone band) was carried out in the left hand. In three other adult control animals, samples for biopsy from the right median nerve were taken at 6 months for histologic evaluation. Six months later, the median nerves were harvested from the eight experimental animals and light and electron microscopic evaluation was carried out studying the nerve proximal and distal to the carpal tunnel, as well as through the carpal tunnel region. Samples for biopsy

### Table I. Morphologic assessment

<table>
<thead>
<tr>
<th>Compression (mo)</th>
<th>Treatment</th>
<th>N</th>
<th>Fiber diameter ($\mu$) ($\pm$ SEM)</th>
<th>Perineurium ($\mu$) ($\pm$ SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3</td>
<td>3</td>
<td>$6.6 \pm 1.3^*$</td>
<td>$6.0 \pm 2.4^*$</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>3</td>
<td>$4.6 \pm 1.6$</td>
<td>$15.0 \pm 2.5$</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>3</td>
<td>$4.3 \pm 0.6$</td>
<td>$16.8 \pm 5.5$</td>
</tr>
<tr>
<td>6 Neurolysis</td>
<td>8</td>
<td>5.2 $\pm 0.5$</td>
<td>$16.8 \pm 2.6$</td>
<td></td>
</tr>
<tr>
<td>6 Decompression</td>
<td>8</td>
<td>4.9 $\pm 0.8$</td>
<td>$13.5 \pm 2.8$</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05.
Fig. 3. A, The normal architecture of the cynomolgous median nerve is demonstrated with the perineurium (arrow) noted and a population of well myelinated fibers. B, After 12 months of nerve compression, thickening of the perineurium and internal epineurium with thinning of the myelin is noted. C, Six months after decompression of the chronically compressed nerve, improved architecture of the median nerve is noted, with thinning of the perineurium and thinning of the internal epineurium. D, Six months after internal neurolysis, there was no histologic difference between this nerve and the nerve that was decompressed. Subperineurial Renaut bodies are noted (arrow). Transverse section. (Toluidine blue stain. Original magnification, ×92.)

were taken from the three animals in which the silicone bands were left on the left median nerve for the full 12 month course of the study. In this study, 12 months of compression would represent the natural progression of untreated compression neuropathy.

**Histologic evaluation.** The median nerves were harvested en bloc beginning proximal to the carpal tunnel and extending distally to the region of nerve compression. These nerves were fixed with Karnowsky’s fixative and postfixed with osmium tetroxide and embedded in Araldite 502 (Ciba-Geigy, Canada). Sections 1 μm were stained with toluidine blue and examined by light microscopy.

Electron microscopic sections were examined on a Philips 300 electron microscope (Philips Electronic Instruments, Mt. Vernon, N.Y.) after lead citrate stained sections were cut with a LKB II ultramicrotome (LKB, Productur, AB Bromma, Sweden).

Morphologic evaluation was carried out by means of digitizing pad (Bioquant II, R & M Biometrics, Nashville, Tenn.), with computerized (IBM) linked digital pen at ×800 magnification. Fiber histograms were obtained and with the use of standard grid areas (37,500 μm²) axon and fiber areas were determined and axon and myelin and axon and fiber ratios were calculated.

**Electrophysiologic studies.** By Teca instrumentation (TECA TE 42), electrophysiologic recordings were carried out at 0, 6, and 12 months and after 6 months of either decompression or internal neurolysis. Motor amplitude and latencies were determined stimulating the nerve proximal to the wrist and recording from the
thenar muscles. Orthodromic sensory recordings were obtained by stimulating the index finger and recording proximally on the median nerve.

Results

After 6 and 12 months of banding of the median nerves, changes were noted in both the nerve fibers and the connective tissue layers of the nerve that were indicative of changes of chronic nerve compression. Morphometric findings are detailed in Tables I and II and graphically in Fig. 4. Thinning of the myelin was noted with subsequent decrease in the percentage of myelin and increase in the axon and myelin and axon and fiber ratios. Thickening of the interfascicular epineurium and perineurium was also noted (Tables I and II, Fig. 4). After 6 months of compression, there was evidence of only mild to moderate compression. After 12 months, severe compression with Wal-
Fig. 5. A, In the normal cynomologous median nerve, a population of well myelinated fibers is seen. B, After 6 months of chronic nerve compression, there is thinning of the myelin. C, After 12 months of chronic nerve compression, progressive thinning of the myelin is noted with an apparent increase in the population of the thinly myelinated small fibers. D, After simple decompression or internal neurolysis, the fiber population demonstrated some thickening of the myelin although the fibers did not return to normal (Fig. 4, A). This micrograph is taken from a neurolysed nerve. Transverse section. (Toluidine blue stain. Original magnification, ×588.)

Table II. Axon:myelin ratio

<table>
<thead>
<tr>
<th>Compression (mo)</th>
<th>Area ± SEM (μ²)</th>
<th>% Myelin</th>
<th>Axon/myelin</th>
<th>Axon/fiber (G-ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Axon</td>
<td>Myelin</td>
<td>Fiber</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>34.6 ± 1.14</td>
<td>57.6 ± 2.3*</td>
<td>92.2 ± 1.13*</td>
<td>63</td>
</tr>
<tr>
<td>6</td>
<td>31.4 ± .87</td>
<td>27.5 ± 1.10</td>
<td>58.9 ± 1.41</td>
<td>46</td>
</tr>
<tr>
<td>12</td>
<td>34.8 ± 1.30</td>
<td>17.9 ± 1.19</td>
<td>52.1 ± 1.55</td>
<td>34</td>
</tr>
<tr>
<td>Neurolysis 6+</td>
<td>27.0 ± 0.01</td>
<td>26.2 ± 0.10</td>
<td>53.3 ± 0.14</td>
<td>50</td>
</tr>
<tr>
<td>Decompression</td>
<td>28.4 ± 0.01</td>
<td>24.8 ± 0.08</td>
<td>53.2 ± 0.19</td>
<td>46</td>
</tr>
</tbody>
</table>

*p < 0.05.

nerve degeneration was noted. After internal neurolysis or simple decompression, histologic evaluation (Figs. 3 and 5) and morphologic assessment (Tables I and II) demonstrated an improvement in all factors measured when comparison was made with those nerves that had been compressed for 6 and 12 months. There was no statistical difference (paired Students t-test) between either treatment group. None of the parameters
measured in either treatment group returned to normal values.

Progressive deterioration of electrophysiologic status was noted in both sensory and motor latency and amplitude after 6 and 12 months of nerve compression. While there was some improvement in these parameters after neurolysis or simple decompression, there was no statistical difference noted between these two treatment groups (Fig. 6).

Discussion

The role of internal neurolysis in the management of the patient with nerve injury is as controversial today as it was when first described in the early 1900s. Several authors support the use of internal neurolysis in the management of carpal tunnel syndrome, however, has cautioned that “inevitable interfascicular scarring can produce irreparable damage to the median nerve” after internal neurolysis. Lundborg, Rydevik, and Nordborg noted that “internal neurolysis per se implies a significant trauma to the nerve and may induce microvascular damage and formation of new intraneural scar tissue.” Hudson et al. concluded that a carefully performed internal neurolysis would not produce “any significant long lasting morphological or physiological alterations in a peripheral nerve.” Both studies were done on normal, subprimate nerves made up of only a few fascicles.

Compression of the median nerve of the cynomolgus monkey, which contains 16 ± 5 fascicles, produces progressive nerve fiber and connective tissue changes at 6 and 12 months. Histologic, morphologic, and electrophysiologic assessment of the two treatment groups demonstrated no difference between these groups but improvement was noted in all parameters when the two treatment groups were compared with the nontreatment group at 6 and 12 months.

In this study, the neurolysis performed was extensive (complete interfascicular epineurectomy) in order to stress the hypothesis that neurolysis would not cause fiber pathology or scarring. In the clinical situation, the appropriate internal neurolysis is a “stepwise” neurolysis preceding from epifascicular epineurectomy to epifascicular neurectomy to partial to complete interfascicular epineurectomy. Thus, frequently the neurolysis required clinically will be far less than that carried out in this study.

In this study, internal neurolysis did not confer improved histologic or electrophysiologic results as compared with simple decompression alone. It is emphasized that neurolysis was carried out after only 6 months of nerve compression. At this time, there was no evidence of Wallerian degeneration (the clinical counterpart being muscle atrophy and abnormal two-point discrimination). Our understanding of the histopathologic picture of chronic nerve compression is a spectrum.
extending from changes in the blood nerve barrier and regional ischemia to Wallerian degeneration. A histologic study of human chronic nerve compression demonstrated that patients complaining of identical symptoms demonstrated very different histologic changes in their nerves. In four human nerves studied, all specimens demonstrated changes in the perineurium and endoneurial microvessels. By contrast, the nerve fibers themselves varied from normal to degenerated in different patients.

Since the clinical correlates of morphometric abnormalities are not known, the experimental design of this study will not permit this data to be interpreted in terms of which treatment group gives better hand function or improved symptoms. While a direct comparison cannot be made between histology, electrophysiology, and nerve function, the results of this study would confirm clinical experience that dictates that in mild to moderate symptoms, simple decompression alone will yield excellent clinical results.

We would like to thank Dr. Raymond M. Curtis for his unlimited enthusiasm and support given in 1981-82 when the preliminary studies leading up to this report were initiated. The authors are indebted to Dr. A. R. Hudson, Professor and Chairman, Division Neurosurgery, University of Toronto, and Dr. W. W. Eversman, Jr., for their critical evaluation of the manuscript and to Mr. Daniel Hunter, electromicroscopist, for his comprehensive tissue evaluation. The authors thank Mr. W. A. Seiler IV, chief microsurgical technician, for his superb help throughout the course of the study, and Mr. R. Schlegel, chief of physical rehabilitation at Union Memorial Hospital, for his technical expertise in carrying out the nerve conduction studies.

REFERENCES