

# Double-crush syndrome:

## A critical analysis

Asa J. Wilbourn, MD, and Roger W. Gilliatt, MD†

In 1973, after assessing a large group of patients with cervical root lesions (CRLs) and upper extremity peripheral entrapment neuropathies—either carpal tunnel syndrome (CTS), ulnar neuropathy at the elbow (UN-E), or both—Upton and McComas<sup>1</sup> proposed that focal compression often occurs at more than one level along the course of a single nerve fiber. They proposed that under these circumstances a disturbance of axonal transport caused by compression at the proximal site (e.g., the cervical root) might impair the capacity of the nerve segment distal to it to resist further focal compressive injury. In this manner, an otherwise subclinical focal entrapment neuropathy (e.g., CTS) could be converted into a clinically evident one (figure 1). They assumed that this may occur even though the proximal lesion, while symptomatic, was not clinically severe. Thus, a cervical radiculopathy manifesting as little more than neck pain and stiffness could still precipitate a distal focal entrapment neuropathy. For this mechanism of nerve injury—serial compromise of axonal transport along the same nerve fiber, causing a subclinical lesion at the distal site to become symptomatic—they proposed the term *double-crush syndrome* (DCS). They acknowledged that this term was too restrictive because (1) the proximal focal disturbance could result from traction, rather than compression; (2) there could be more than two sites of injury along an axon; and (3) a generalized subclinical polyneuropathy, by reducing the amount of “trophic material manufactured by the perikaryon” in all peripheral nerve fibers, could serve as the proximal compression site.<sup>1</sup>

In support of this theory, they reported that a large series of their patients with CTS and UN-E had a high occurrence of CRLs, according to clinical, EMG, and radiologic data. Of the 115 patients with one or more distal entrapment neuropathies in one or both limbs, a coexisting cervical radiculopathy was “probable” in 81 (70%) and “possible” in an additional five patients (4%).<sup>1</sup> How these nerve lesions were established is pertinent. All entrapment neuropathies were confirmed by electrodiagnostic (EDX) examinations that demonstrated focal slowing on nerve conduction studies (NCS), whereas only some of the cervical radiculopathies were verified by the

presence of denervation in the myotome distribution on needle electrode examination (NEE); the others were diagnosed inferentially, based on clinical and radiologic changes.<sup>1</sup>

Since its inception, DCS has become widely accepted. Nonetheless, serious questions can be raised about this concept in terms of its experimental supporting data and certain anatomic, pathologic, and pathophysiologic aspects of its clinical application.

**Experimental aspects.** Considering how clinically pervasive DCS has become, relatively little experimental work has been performed to validate it. One question that research has attempted to address is whether the amount of nerve injury caused by double or multiple lesions of a single nerve pathway merely represents the additive effects of independent lesions or materially exceeds what was expected. A second question is whether the initial lesion causes the remaining nerve segment to be more vulnerable to a second focal injury by sensitizing it in some manner.

Probably the most widely quoted experimental study focused on DCS was reported by Nemoto et al.<sup>2</sup> in 1987. In their report, assessing acute and subacute nerve lesions, small spring clips exerting a force of approximately 15 g were placed on the sciatic nerves in the upper thighs of dogs, which were divided into two groups. In the first group, only one clamp was applied. In the second, an additional clamp was put into place 3 weeks after the first one and 2 cm distal. The clamps were left in situ in both groups for 8 weeks after the initial procedure. At intervals during the experimental period, motor NCS were carried out using percutaneous needles for sciatic nerve stimulation and for recording from the tibialis anterior muscle. In the first group the nerve was stimulated proximal and distal to the single clamp. In the second group the nerve stimulations were applied proximal to the first clamp and distal to the second one. The histologic changes were assessed at the end of the study.<sup>2</sup>

The most easily established conclusion from this study is that the addition of a second clamp produced a combined deficit that greatly exceeded that produced by a single clamp alone. For the single lesion, a partial conduction block was the rule; complete

†From the Department of Neurology, Cleveland Clinic Foundation, Cleveland, OH.

Deceased.

Received December 27, 1996. Accepted in final form December 27, 1996.

Address correspondence and reprint requests to Dr. Asa J. Wilbourn, EMG Laboratory-Desk S90, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.

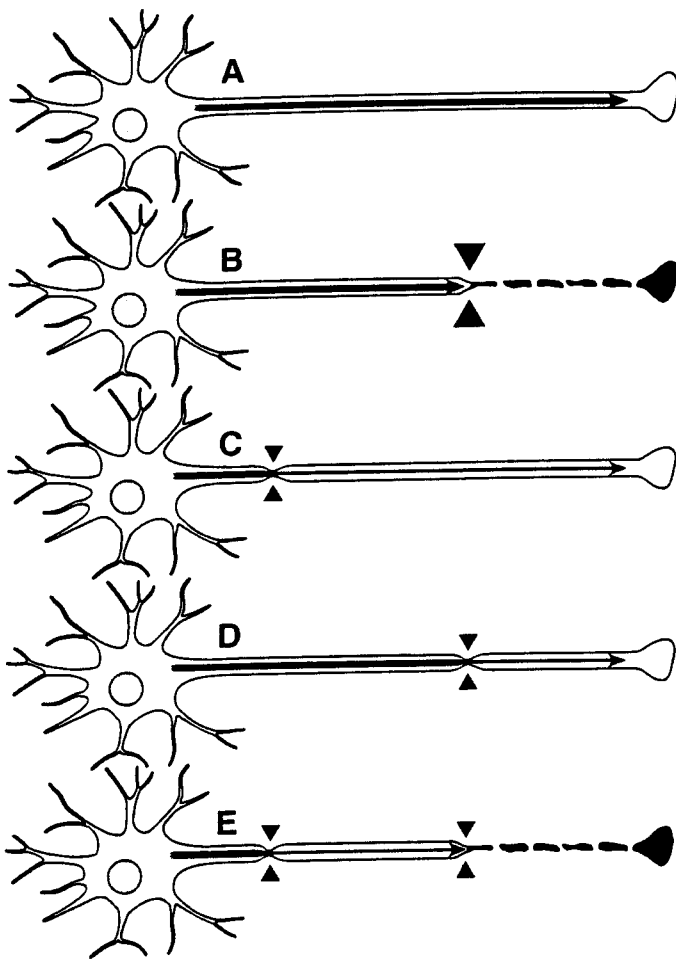


Figure 1. Diagram of the double-crush hypothesis of Upton and McComas. Shown is the perikaryon and axon, with the antegrade axoplasmic flow represented by an arrow (thickness of the arrow indicates amount of transported material). (A) Normal. (B) Severe distal injury causing axon death with degeneration. (C) Mild proximal compression causing only impairment of axoplasmic flow. (D) Mild distal lesion causing only impairment of axoplasmic flow. (E) Combined mild proximal and distal lesions with sequential axoplasmic flow impairments culminating at distal lesion site and causing axon death with degeneration. (From Upton and McComas,<sup>1</sup> with permission.)

blocks did not occur. Across the double lesion, however, conduction was reportedly blocked completely in 50% of the experiments. Histologic studies also emphasized the greater severity of the changes with paired lesions, although the reported loss of myelinated fibers in the distal segment of the nerve was not quantified with nerve fiber counts.<sup>3</sup> Unfortunately the conduction across the second (distal) lesion was not measured directly, with stimulation between the two clamps. The question that should have been asked was whether the second (distal) clamp produced a disproportionate effect compared with the first (proximal) one. Unable to establish this point, Nemoto et al.<sup>2</sup> could only suggest that it might have occurred, because according to them, the overall reduction in maximum motor conduction velocity (CV) across the two lesions was more than twice that ob-

served along the proximal one alone (14% of normal versus 37% of normal), and a complete conduction block was found only when two lesions had been created. However, these findings cannot be taken as evidence of an exaggerated effect of the distal compression for two reasons. First, there are problems in regard to neurophysiologic terminology and concepts. They report that in 50% of the nerves in the second group "complete conduction block" was induced, but they define the latter as "25% being the first degree injury and 25% being the second degree nerve injury after Sunderland."<sup>2</sup> However, Sunderland's<sup>4</sup> second-degree injury is not a demyelinating conduction block at all, but rather the type of axonal loss in which the supporting structures of the nerve at the lesion site remain intact, termed *axonotmesis* by Seddon<sup>5</sup> in his classification of peripheral nerve injuries. In other words, in the second group of experimental animals, 25% of the axons distal to the lesion site underwent Wallerian degeneration. Moreover, to obtain the very slow CV reported at the distal site (14% of normal), the authors chose to consider the CV as "0 m/sec" whenever complete "conduction block" (their definition) was present. This approach is not one customarily used in such circumstances. Whenever a response cannot be elicited on nerve stimulation, due to either conduction failure resulting from Wallerian degeneration or conduction block due to demyelination, a CV cannot be determined, because conduction is not occurring. Therefore, such NCS results are excluded from consideration. They cannot arbitrarily be assigned a "0 m/sec" CV, and then have such included in the pooled CV data, as this results in materially lowering the average CV, as occurred in this case. When the results from those animals with "complete conduction block" were excluded, the mean CV in the double-clamp group was 33% of the preoperative value, close to the 37% obtained in the single-clamp experiments. Second, as Swensen<sup>3</sup> has noted, the experimental design is not similar to the clinical DCS. In the second group the clamps were applied so close to one another that the blood flow in the intervening segment likely was compromised, and many of the effects that occurred were possibly caused by the resulting ischemic lesion.

Mackinnon, Dillon, and others<sup>6-11</sup> performed a series of experiments on chronic constriction and its summation when applied at different levels along nerve fibers. They used Silastic cuffs to obtain gradual constriction of the sciatic nerve in the rat. Each piece of Silastic tubing was opened down its length (0.5 to 1 cm) before being sutured in place around the nerve. Its internal circumference at the beginning of the experiment was sufficient to fit around the nerve snugly without applying pressure. Constriction appeared to develop gradually, presumably in association with growth of the underlying nerve, resulting in a chronic, progressive, focal neuropathy with local demyelination, remyelination, large fiber loss, endoneurial fibrosis, and perineurial thicken-

ing. In their most recent paper,<sup>6</sup> the authors placed Silastic cuffs around the sciatic nerve above its trifurcation, or around the tibial nerve, just below its origin. In one group of animals, both proximal and distal cuffs were applied together; in others, a proximal or distal cuff was added to the other after an interval of several months. The effect of constriction was assessed over a period of 1 year by monthly measurement of nerve CV and nerve action potential (NAP) amplitude with stimulation proximal to the sciatic cuff, while recording distal to the tibial cuff. Although the histologic findings after banding were described in detail by others, these were not used to quantify the effect of single and double constriction in the most recent paper. Reliance was placed solely on the NCS.

The main result of these studies may be summarized as follows. In the animals with a single cuff on either the sciatic or tibial nerve there was, after 5 months, a fall in the NAP amplitude and in the nerve CV (NCV), which was less than that occurring in the double lesions that had been made together at the onset of the experiments. If the groups with single lesions were followed for 7 months and then second bands applied, the results by the end of the first year were similar to those obtained by making the double (proximal and distal) lesions at the onset. Thus, with single banding the NAP amplitudes decreased 1 to 1.5 mV and the NCVs decreased between 10 and 13 m/per second. Conversely, with double banding the NAP amplitudes decreased approximately 2.5 mV, while the NCVs decreased approximately 16 m/per second.<sup>6</sup>

In other words, no exaggeration in the combined lesions was obtained by making the distal lesion late, rather than at the same time or in advance of the proximal one. These results suggest that two independent constrictions along nerve pathways summate their effects so that the overall change is greater than that caused by either independently. However, the fact that there was no difference in outcome when the proximal and distal cuffs were placed at the same time or sequentially (in either order) contradicts the hypothesis of Upton and McComas,<sup>1</sup> which implies that the effect of a distal constriction should be greater when it occurs in the presence of a proximal one. There are, in addition, some questions that must be raised concerning the design of these experiments, particularly in regard to the NCS. How old, for example, were the animals at onset, and how much nerve growth would be expected with the cuffs *in situ*? Why were NAP amplitudes measured for a centrifugal rather than a centripetal volley, with all the inherent risks of unwanted muscle action potentials contaminating the nerve response? Should NAP area rather than amplitude have been measured? Why was there no attempt to record the effect of a distal cuff directly, by stimulating and recording across it, rather than across both cuffs together? Is it possible that with this last-mentioned modification of technique a

smaller transient effect of the proximal cuff in exaggerating the effect of the distal one might have occurred?

A series of experiments performed on rabbits and guinea pigs by Gilliatt and others<sup>12-16</sup> to determine the distal changes in nerve fibers after proximal conduction block or constriction yielded information that has some bearing on DCS. They demonstrated that when double lesions occur along nerve fibers, the distal axons may be more susceptible to injury, but only "under strictly circumscribed conditions".<sup>14</sup> Thus, in one study axon regeneration following nerve crush was not impeded when it occurred distal to a prolonged demyelinating conduction block.<sup>16</sup> However, in other studies abnormalities developed in axons situated distal to a constricting nerve lesion. For this to occur, the chronic proximal nerve constriction had to cause a reduction in the caliber of the distal axon (axonal atrophy), which also became morphologically abnormal, with buckling and irregularity of the redundant myelin. This process was accompanied by a reduction in motor CV. The key factor in the production of axonal atrophy distal to a constriction was the severity of the constriction. The best results occurred when silk ligatures were tied around the sciatic or proximal tibial nerve trunks tightly enough to cause most of the large myelinated fibers to degenerate completely at the lesion site. Studies could then be performed on the minority of fibers that survived without degeneration and were confined proximally by the ligature. This experimental model demonstrated that demyelination (mainly paranodal) occurred in the atrophic fibers distal to the constriction. In one group of animals constriction was apparently associated with secondary demyelination and recent Wallerian degeneration, which had not occurred at random throughout the distal part of the constricted fibers. Instead, these particularly affected plantar nerve fibers in the sole of the foot, suggesting that those abnormal axons might have been "particularly sensitive to local pressure".<sup>15</sup> Still another study<sup>14</sup> demonstrated that when atrophic nerve fibers distal to a persistent constriction were crushed, the time required for muscle reinnervation was delayed, as demonstrated both by histologic and NCS results, suggesting nerve regeneration was impaired.

This series of experiments suggest that atrophic axons have an increased susceptibility to pressure. A major reservation in respect to this conclusion as it pertains to DCS, however, is the severity of constriction needed to produce a positive result in the animals studied. If most of the large myelinated fibers (>80%) must undergo acute axon degeneration at the proximal lesion site before the surviving fibers demonstrate axonal atrophy and an increased vulnerability to trauma distally, this very probably is not a mechanism that is of practical importance in humans, particularly in regard to DCS, in which the proximal lesions often are reported as subclinical.

Finally, in a brief report, Trontelj et al.<sup>17</sup> demon-

**Table** Some various combinations of nerve lesions reported in the literature as instances of double-crush syndrome

Proximal nerve	Distal nerve	Reference	
Mental nerve	Inferior alveolar n.	18	
C5, C6 myelopathy	Axillary n.	19	
Cervical root	Brachial plexus (TOS)	20	
	Long thoracic nerve	21	
	Median n., wrist (CTS)	1,7,11,21-35	
	Median n., elbow (AIN)	34,36	
	Ulnar n., elbow	1,7,11,21,29-32,34,37-40	
	Ulnar n., wrist	34,39	
	Radial n., elbow (e.g., radial tunnel, PIN)	21,31,32,34	
	Brachial plexus (mostly TOS)	Median n., wrist (CTS)	11,20,25,28,29,31,32,34,41-49
		Median n., elbow	48-50
		Ulnar n., elbow	11,20,29-32,34,39,41,42,44,48,49,51-53
Ulnar n., wrist		20,34,39,48	
Radial n., elbow (e.g., radial tunnel, PIN)		20,54	
Median nerve, elbow (e.g., pronator syndrome)	Median n., wrist (CTS)	11,21,32,34,56-58	
Ulnar nerve, elbow	Ulnar n., wrist	30,32,34,39,59	
Radial nerve, elbow	Radial n., elbow	60	
Lumbosacral root	Femoral n.	34	
	Peroneal n., fibular head	29,32,34,61	
	Tibial n., popliteal fossa	34	
	Tibial n., foot (TTS)	32,34,62,63	
	Tibial nerve, leg	Tibial n., foot (TTS)	63

n. = nerve; TOS = thoracic outlet syndrome; CTS = carpal tunnel syndrome; AIN = anterior interosseous nerve; PIN = posterior interosseous nerve; TTS = tarsal tunnel syndrome.

strated along single human axons two separate regions of CV slowing, with the proximal one corresponding to a root or plexus lesion and the distal one occurring at a site of nerve entrapment (median nerve at carpal tunnel, ulnar nerve at elbow). No details are provided regarding the techniques used.

In summary, no published experimental studies to date have shown that dual lesions along nerve fibers cause magnified damage, nor have any demonstrated that the segment of nerve distal to a focal lesion is, in the DCS context, particularly susceptible to an additional focal insult. What has been proved is that consecutive focal lesions along a nerve may have an additive effect. It is also interesting to note that with most of the experimental models the second lesion has been manifested as focal slowing, presumably secondary to demyelination, yet the DCS hypothesis requires that the distal lesion result in axonal loss.<sup>1</sup>

**Clinical aspects.** DCS is encountered with some frequency in the current literature, particularly in surgical publications. Nearly 20 different combinations of nerve fiber lesions have been designated as examples of DCS (table). Most of these pairings have involved upper extremity nerve fibers, usually with the proximal injury being at the root or plexus level, and the distal injury located along one of the main

peripheral nerves of the limb. One of the most commonly described associations has been CRL and CTS, as initially reported by Upton and McComas.<sup>1,7,11,21-35</sup> Less often, CRL had been linked to UN-E,<sup>1,7,11,21,29-32,34,37-40</sup> as well as to anterior interosseous neuropathies (AIN),<sup>34,36</sup> ulnar neuropathies at the wrist (UN-W),<sup>34,39</sup> and to radial neuropathies near the elbow.<sup>21,31,32,34</sup> Various elements of the brachial plexus also frequently have been designated as the proximal lesion site. The types of plexus lesions mentioned have included neuralgic amyotrophy<sup>28,41</sup>; traumatic,<sup>41</sup> radiation-induced,<sup>41</sup> axilla compression<sup>42</sup>; and, particularly, the disputed type<sup>64</sup> of thoracic outlet syndrome (TOS).<sup>7,11,20,25,29-32,34,37,39,40,43-54</sup> In most instances these brachial plexopathies have been linked to CTS.<sup>11,20,25,29,31,32,34,41-49</sup> However, they also have been paired with UN-E,<sup>11,20,29-32,34,37,39,41,42,44,48,49,51-53</sup> with UN-W,<sup>20,28,39,48,49</sup> with median neuropathies at the elbow (including AIN),<sup>34,48-60</sup> and with radial neuropathies at the elbow.<sup>20,48,54</sup> Dual lesions also have been reported along several upper extremity nerves, including the median (pronator syndrome and CTS),<sup>11,31,34,56-58</sup> ulnar (UN-E and UN-W),<sup>31,32,39,59</sup> and the posterior interosseous nerves.<sup>60</sup>

Very few reports of DCS occurring beyond the upper extremity have appeared. Nonetheless, their existence was predicted as early as 1977.<sup>29</sup> Similarly,

Shapiro et al.<sup>34</sup> were convinced of the ubiquity of this mechanism of nerve injury in 1993: "Although the double-crush lesion in the lower extremity has not been described, it does exist."<sup>34</sup> In fact, one such report had appeared in 1985,<sup>62</sup> a few others have followed,<sup>34,61,63</sup> and Shapiro et al.<sup>34</sup> added some theoretical ones. In most instances the proximal lesion has involved the lumbosacral roots, while the distal one affected the peroneal nerve at the fibular head<sup>29,32,34,61</sup> or the tibial nerve, either in the popliteal fossa<sup>34</sup> or at the ankle (tarsal tunnel syndrome).<sup>32,62,63</sup> Dual lesions of the tibial nerve in the popliteal fossa and at the ankle have also been reported.<sup>63</sup>

Some of the more exotic combinations of nerve lesions attributable to DCS have included CRL with TOS,<sup>20</sup> CRL with a long thoracic neuropathy,<sup>21</sup> a C5, myelopathy with an axillary neuropathy,<sup>19</sup> and inferior alveolar neuropathy with a mental neuropathy.<sup>18</sup>

A theme common to many of these publications is that DCS is the explanation for an unexpected surgical result: either an operative nerve decompression that, although considered technically satisfactory, did not relieve the patient's symptoms<sup>6,18,23-25,32-39,40,44,45,54,65,72</sup> or the sudden appearance, in the post-operative period, of a nerve lesion that was not present prior to surgery.<sup>18,53,61,66</sup> Thus, hand symptoms in a median nerve distribution that are unrelieved by CTS surgery are attributed to a coexisting CRL or TOS,<sup>23,24,44,65</sup> while a peroneal neuropathy that is first evident following total knee arthroplasty is linked to a prior lumbosacral radiculopathy.<sup>61</sup>

Since its debut, the DCS has undergone several transformations and expansions. A "reversed DCS" has been postulated, whereby a distal lesion (e.g., UN-W) triggers a more proximal lesion (e.g., UN-E) by compromising retrograde axoplasmic flow.<sup>39,59</sup> Moreover, at least seven other etiologic mechanisms have been proposed to explain the relationship between the proximal and distal nerve fiber lesions<sup>1,28,32,59,67-71</sup>:

1. A proximal nerve lesion renders the distal nerve segment more vulnerable to compression due to serial constraints of axoplasmic flow. The peripheral nerves possess an underlying susceptibility to pressure.
3. Interruption of lymphatic/venous drainage at the proximal nerve lesion site renders the distal nerve segment more vulnerable.
4. Endoneurial edema at one lesion site compromises neural circulation, rendering nerve fibers at the other site more vulnerable.
5. A connective tissue abnormality is common to both sites along the nerve fibers. Tethering of the nerve at one site causes injurious shear forces at the other site.
7. Entrapment of the nerve at one site causes decreased use of the muscle pump, which creates a slight, generalized edema of limb. This increases tissue pressure in certain anatomic passages,

which causes an additional entrapment nerve lesion.

8. The initial nerve lesion releases a metabolite that passes through the "free intraneural circulation" and increases the vulnerability of other segments of the nerve.

Nonetheless, the original theory of Upton and McComas—serial constraints of axoplasmic flow—remains the most popular hypothesis, and this discussion will focus solely on it.

Some investigators, as Upton and McComas<sup>1</sup> envisioned in their original paper, have taken the DCS concept further and have described "triple-crush" and even "quadruple-crush" or "multiple-crush" syndromes.<sup>7,20,32,40,44,48,49</sup> In these instances, symptoms that formerly would have been attributed to a single focal disorder are now thought to result from a series of coexisting, often subclinical, lesions along the peripheral nerve fibers, either at different levels or in the same region, each of which is assumed to contribute to the symptomatology and each of which requires therapy, with the latter frequently consisting of surgical decompression. At least 10 potential compressive structures have been listed for the brachial plexus in the thoracic outlet; nine for the median nerve in the proximal forearm; six for the ulnar nerve in the arm, forearm, and hand; as well as six for the radial nerve in the arm and proximal forearm.<sup>40,72</sup> In this regard, Dillon and Mackinnon<sup>6</sup> have stated that patients with "complex trauma" of the upper extremity may potentially have their nerve fibers injured at multiple points, including the roots, various sites within the brachial plexus, the ulnar nerve at the elbow, the median and ulnar nerves at the wrist, and the superficial radial nerve in the forearm. They note further that "... patients should be prepared to have additional sites decompressed ... as the most obvious site of compression is relieved."<sup>6</sup> An incidental effect of this theory is that it provides an acceptable explanation for two or even more failed operative procedures performed to treat essentially the same symptoms. In the pre-DCS era, such unsuccessful results would have raised serious concerns regarding the diagnostic or technical skills of the surgeon.

It is rather ironic that surgery has come to play such a dominant role in the treatment of DCS, considering that the hypothesis of Upton and McComas regarding the association of two-level nerve lesions was modeled in part after one proposed earlier (in 1961) by Lishman and Russell,<sup>67</sup> who were fervent advocates of conservative treatment for both CRLs and entrapment neuropathies. Using resting of the limb as the centerpiece of their therapy, they successfully treated most of their patients. They noted that only a few required carpal ligament release and none needed cervical root or thoracic outlet operations. How successful they were at medical prognostication, however, must be judged by their statement: "Indeed, we are doubtful whether the present

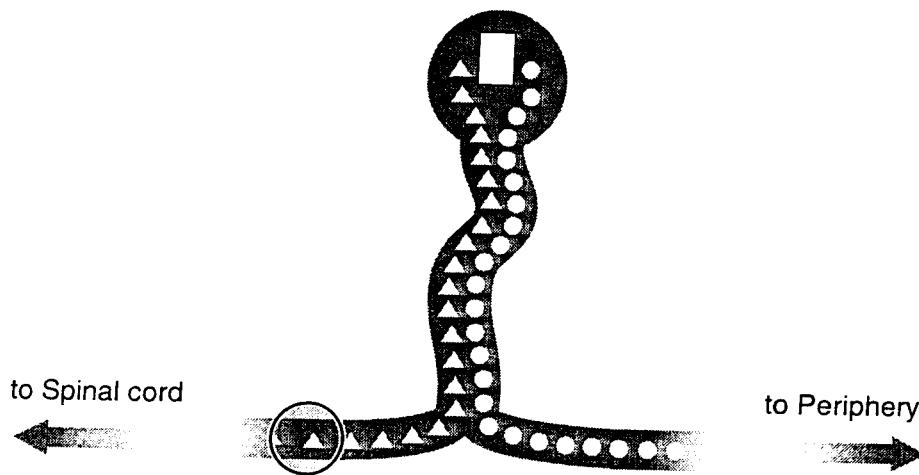


Figure 2. Diagram of a unipolar sensory cell in the dorsal root ganglion, with its two branches, one passing centrally (dorsal root branch) to the spinal cord and the other passing peripherally. The typical site of injury along the sensory pathway with a compressive radiculopathy is shown (gray circle) on the dorsal root branch. The different axoplasmic flow systems in the two branches are also indicated (triangles, small circles).

enthusiasm for operating either on the carpal tunnel in Britain, or on the cervical nerve roots in the United States, will last".<sup>67</sup>

As a consequence of it linking lesions at more than one site along peripheral nerve fibers, including some lesions that may be controversial (e.g., disputed neurologic TOS)<sup>2,6,34,44,72</sup> as well as subclinical, the DCS concept has entered the realm of personal injury litigation. Thus, in one recently published book (1993) dealing with the legal consequences of trauma, an entire chapter is devoted to DCS and focuses on the various types of combined nerve lesions that might occur, as well as the "distribution of responsibility for the individual lesions and determination of liability for combined lesions."<sup>34</sup>

Few challenges to the DCS have appeared, and most have been limited.<sup>3,73-75</sup> An exception is the article by Carroll and Hurst,<sup>76</sup> in which they reported finding TOS and CTS together in patients so seldom that they did not consider this pairing a representative example of DCS.

In view of its popularity, one could assume that the DCS imposes few restrictions on its application. In fact, however, it has certain requisites that should severely limit its use. On review of the clinical examples of DCS cited in the literature, it is obvious that these requirements very often are ignored. The tenet most often breached is the most basic one: that there be anatomic continuity of nerve fibers between the two (or more) lesion sites. If this is lacking, then sequential impairment of axoplasmic flow obviously cannot occur. Consequently, two focal nerve disorders along the same neural pathway (e.g., CRL and CTS) do not automatically fulfill this anatomic criterion of DCS; only if the same axons are compromised at both sites is this the result. This requirement is the major impediment to acknowledging as authentic most of the reported clinical examples of DCS. It poses difficulties for the DCS in two separate contexts: (1) whenever the proximal lesion is situated within the intraspinal canal (e.g., with radiculopathies) and (2) whenever the distal lesion affects a peripheral nerve structure that has an extensive proximal origin (e.g., the median nerve at the wrist).

Lesions within the intraspinal canal are in compliance with the DCS hypothesis whenever they affect motor fibers. They are not in compliance, however, when they involve sensory fibers. This is because they injure the sensory fibers proximal to their cell bodies of origin in the dorsal root ganglion (DRG), in contrast to the more distally situated lesions (e.g., plexus or peripheral nerve) that damage the postganglionic sensory fibers.<sup>77</sup> The pre- and postganglionic sensory fibers are not anatomically continuous, even though they share the same unipolar cell body. Injury to one of them, regardless of severity, has no effect on the other, unless there is concomitant damage to their common cell body in the DRG (figure 2). This fact has been well-known to electromyographers since Bonney and Gilliatt<sup>78</sup> demonstrated in 1958 that on NCS the sensory responses, unlike the motor, are not altered by root avulsion injuries because preganglionic sensory fibers are damaged. Thus, a root avulsion that destroys virtually all the C8 root fibers has no effect on the ulnar sensory NCS amplitude, even though the sensory axons assessed are derived from the C8 DRG and there is a marked clinical sensory deficit in a C8 dermatomal distribution.<sup>79</sup> The independence of the centrally and peripherally directed sensory branches of the DRG cells extends to their axoplasmic transport systems. Ochs et al.<sup>80,81</sup> have shown that the amount and type of material passing down them differs. For example, approximately three to five times more labeled material is transported into the peripheral fibers compared with the dorsal root fibers. Therefore, regardless of how severely damaged the dorsal root fibers (and their axoplasmic transport systems) are by a compressive radiculopathy, the axoplasmic flow systems of the unaltered peripheral sensory fibers remain normal, because the continuity of these axons with their cell bodies is not disturbed. With these facts in mind, it is obvious that a radiculopathy can never be the proximal lesion with a DCS if sensory abnormalities, clinically or on NCS, are to result from the addition of a distal lesion, since the sensory axons will have been injured at only one site (i.e., distally) rather than the two required. Yet, sensory

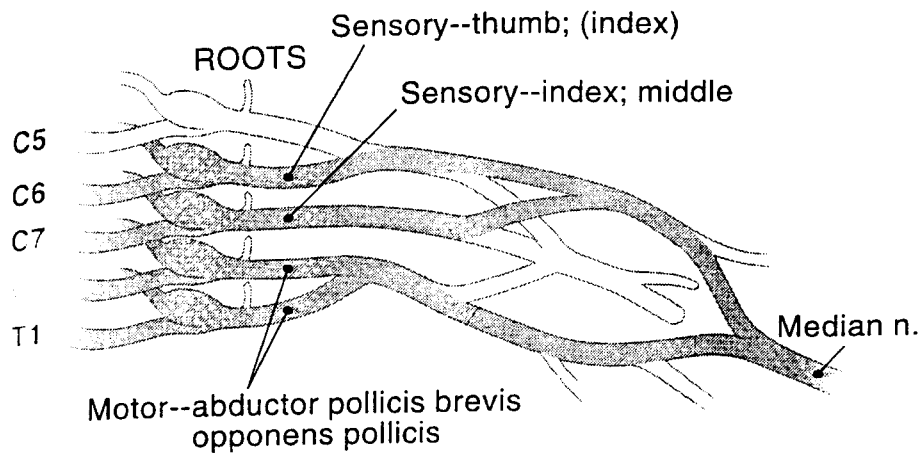


Figure 3. Illustration of brachial plexus showing pathways followed by median motor and sensory fibers that traverse the carpal tunnel to innervate the hand. The motor pathways are generally accepted; the sensory pathways are those provided by Ferrante and Wilbourn.<sup>55</sup>

disturbances are prominent in most situations in which CRLs and distal entrapment neuropathies are required, and are labeled as instances of DCS.

The fibers composing the radial nerve in the arm and the median nerve throughout nearly all of its course are widely distributed at the root and plexus levels. The median nerve has the most extensive proximal origin of any upper extremity nerve. Its fibers, including those that traverse the carpal tunnel, originate from four separate roots (C6, C7, C8, and T1) and traverse all three trunks (upper, middle, lower) and two of the three cords (lateral and median) of the brachial plexus (figure 3). Consequently, of all peripheral nerves, the median is probably the one most unsuitable to serve as the site of the distal lesion with DCS, if the proximal lesion is to be at the root or plexus level. Under these circumstances, to damage all the axons proximally that are compromised distally requires a widespread proximal lesion, one that simultaneously affects four separate cervical roots or most of the brachial plexus elements. Chronic lesions of this magnitude are almost always axonal loss in type and severe in degree. In the literature such injuries are rarely designated as the proximal lesion with DCS. They are not only relatively rare but they also, most definitely, are never subclinical. Instead, they inevitably cause diffuse substantial deficits in the limb and in the distribution of multiple peripheral nerves, rather than in just the median nerve alone.

Another barrier to the application of the DCS hypothesis pertains to the type of nerve pathology that occurs at the distal lesion site as a result of impaired axoplasmic flow. According to Upton and McComas,<sup>1</sup> this is axonal loss. Yet certain entrapment neuropathies are manifested as conduction slowing or, less often, conduction block, both of which are pathophysiologic changes attributed to focal demyelination. In contrast, axonal degeneration causes conduction failure, which has a much different appearance on EDX examination.<sup>79</sup> Concerning the two most common distal entrapment neuropathies associated with DCS: (1) CTS characteristically produces focal slowing, manifested as prolonged latencies, until it is rather advanced; and (2) UN-E causes various combinations

of demyelinating conduction slowing, conduction block, and axonal loss/conduction failure, with the pathophysiology solely that of demyelination in approximately half of the cases.<sup>79,82,83</sup>

Interestingly, even the examples supplied by Upton and McComas in their initial publication on DCS are not in compliance with their hypothesis, because they accepted the diagnosis of the distal lesions (CTS and UN-E) only "if there was evidence of significant slowing of impulse conduction in the potentially vulnerable regions of the median and ulnar nerves (i.e., wrist or elbow, respectively)."<sup>71</sup> They said nothing about finding evidence of denervation on NEE or on NCS, limited to the appropriate median or ulnar nerve distributions.

When all of these restrictions on the DCS are considered, it is apparent that this hypothesis is invoked clinically far more often than is warranted. If the original concepts of Upton and McComas are to be retained, DCS cannot be operable whenever a radiculopathy is the proximal lesion or when the distal injury produces focal demyelination rather than axonal loss. Also, if one of the lesions affects the median nerve or radial nerve proper, the other should not be at the plexus or root level, because it would have to be unusually extensive. Thus, most of the dual nerve lesions listed in the table are not compatible, in one manner or another, with DCS. The often-alluded-to combination of CRL and CTS merits special comment because it is difficult to conceive of two nerve lesions that, when paired together, are more ill suited to be representatives of DCS. Characteristically, CTS is clinically dominated by sensory complaints, and yet root lesions do not affect the peripheral sensory fibers, so their axoplasmic flow is not compromised proximally and, therefore, the distal lesion along them should remain subclinical. The median motor and sensory nerve fibers entrapped at the carpal tunnel are so widely distributed at the root level that only under exceptional circumstances might they all be injured simultaneously. Finally, of all entrapment neuropathies, CTS most consistently causes focal demyelination, and yet the distal lesion with DCS, as defined, produces denervation (axonal

loss). The marked limitations of this clinical example of DCS are discussed at length elsewhere.<sup>84</sup>

Pairing a brachial plexopathy (e.g., disputed neurologic TOS) with CTS eliminates the quandary caused by the location of the lesion along the sensory root fibers, but leaves intact the daunting requirements concerning the extensiveness of the proximal lesion and the pathophysiology produced at the distal lesion site.

An additional problem with the CRL-CTS linkage concerns clinical symptomatology. It seems most improbable to us that a CTS, with its characteristic clinical features (e.g., the onset of nocturnal discomfort in the hands early in the course of the disease), could be precipitated and then mimicked throughout its course by a combination of a constriction at the root or plexus level plus some of the peripheral factors that might lead to an entrapment neuropathy. At most it would seem that invoking the double-crush mechanism could only be justified whenever the clinical presentation was in some manner quite atypical for CTS, and far more so than has been described.<sup>31</sup>

In summary, DCS has many features that sharply limit its clinical use. The fact that it is cited far more frequently than can be anatomically or pathophysiologically justified suggests that it is a concept that gained early, uncritical acceptance, possibly because, as Payan noted, the term *double-crush* is a "pleasing alliteration."<sup>75</sup>

## References

1. Upton RM, McComas AJ. The double crush in nerve entrapment syndromes. *Lancet* 1973;11:359-362.
2. Nemoto K, Matsumoto N, Tazaki K, Horiuchi Y, Uchinshi K, Mori Y. An experimental study on the "double crush" hypothesis. *J Hand Surg Am* 1987;12:552-559.
3. Swensen RS. The "double crush" syndrome. *Neurol Chron* 1994;4:1-6.
4. Sunderland S. Nerve and nerve injuries. 2nd ed. Edinburgh: Churchill-Livingstone, 1978.
5. Seddon HJ. Three types of nerve injuries. *Brain* 1943;66:237-288.
6. Dellon AL, Mackinnon SE. Chronic nerve compression model for the double crush hypothesis. *Ann Plast Surg* 1991;26:259-264.
7. Mackinnon SE, Dellon AL. Surgery of the peripheral nerve. New York: Thieme-Stratton, 1988.
8. Mackinnon SE, Dellon AL. Experimental study of chronic nerve compression. *Hand Clin* 1986;2:639-650.
9. Mackinnon SE, Dellon AL, Hudson AR, Hunter DA. Chronic nerve compression—an experimental model in the rat. *Ann Plast Surg* 1984;13:112-120.
10. O'Brien JP, Mackinnon SE, MacLean AR, Hudson AR, Dellon AL, Hunter DA. A model of chronic nerve compression in the rat. *Ann Plast Surg* 1987;19:430-435.
11. Seiler WA, Schlegel R, Mackinnon S, Dellon AL. Double crush syndrome: experimental model in the rat. *Surg Forum* 1983;34:596-598.
12. Baba M, Fowler CJ, Jacobs JM, Gilliatt RW. Changes in peripheral nerve fibers distal to a constriction. *J Neurol Sci* 1982;54:197-208.
13. Baba M, Gilliatt RW, Jacobs JM. Recovery of distal changes after nerve constriction by a ligature. *J Neurol Sci* 1983;60:235-246.
14. Reiners K, Gilliatt RW, Harding AE, O'Neill JH. Regeneration following tibial crush in the rabbit: the effect of proximal constriction. *J Neurol Neurosurg Psychiatry* 1987;50:6-11.
15. Shimpo T, Gilliatt RW, Kennett RP, Allen PJ. Susceptibility to pressure neuropathy distal to a constricting ligature in the guinea-pig. *J Neurol Neurosurg Psychiatry* 1987;50:1625-1632.
16. Williams IR, Gilliatt RW. Regeneration distal to a prolonged conduction block. *J Neurol Sci* 1977;33:267-273.
17. Trontelj JV, Dolenc V, Janko M. Single axon evidence of double compression mechanism in some entrapment neuropathies. *Acta Neurol Scand* 1979;60(suppl 73):125.
18. Posnick JC, Al-Qattan MM, Stepner NM. Alteration in facial sensibility in adolescents following sagittal split and chin osteotomies of the mandible. *Plast Reconstr Surg* 1996;97:920-927.
19. Adair WA, Schwartz G. Acquired isolated axillary neuropathy: an unusual complication of quadriplegia. *Arch Phys Med Rehabil* 1985;66:713-716.
20. Narakas AO. The role of thoracic outlet syndrome in double crush syndrome. *Ann Hand Surg* 1990;9:331-340.
21. Liveson J. Peripheral neurology: case studies in electrodiagnosis. 2nd ed. Philadelphia: FA Davis, 1991.
22. Cassvan A, Rosenberg A, Rivera LF. Ulnar nerve involvement in carpal tunnel syndrome. *Arch Phys Med Rehabil* 1986;67:290-292.
23. Eason SY, Belsole RJ, Greene TL. Carpal tunnel release: analysis of suboptimal results. *J Hand Surg Br* 1985;10:365-369.
24. Howard FM. Controversies in nerve entrapment syndromes in the forearm and wrist. *Orthop Clin North Am* 1986;17:375-381.
25. Hirsh LF, Thanki A. Carpal tunnel syndrome. *Postgrad Med* 1985;77:185-192.
26. Hurst LC, Weissberg D, Carroll RE. The relationship of the double crush to carpal tunnel syndrome (an analysis of 1,000 cases of carpal tunnel syndrome). *J Hand Surg Br* 1985;10:202-204.
27. Kuntzer T. Carpal tunnel syndrome in 100 patients: sensitivity, specificity of multi-neurophysiological procedures and estimation of axonal loss of motor, sensory and sympathetic median nerve fibers. *J Neurol Sci* 1994;127:221-229.
28. Massey EW, Riley TL, Pleet AB. Coexistent carpal tunnel syndrome and cervical radiculopathy (double crush syndrome). *South Med J* 1981;74:957-959.
29. McComas AJ. Neuromuscular function and disorders. London: Butterworths, 1977:253-259.
30. Nakano KK. The entrapment neuropathies. *Muscle Nerve* 1978;1:264-279.
31. Osterman AL. The double crush syndrome: cervical radiculopathy and carpal tunnel syndrome. *Orthop Clin North Am* 1988;19:147-155.
32. Osterman AL. Double crush and multiple compression neuropathy. In: Gelberman RH, ed. Operative nerve repair and reconstruction. Philadelphia: JB Lippincott, 1991;2:1211-1229.
33. Parachuri R, Adams EM. Entrapment neuropathies. *Postgrad Med* 1993;94:39-57.
34. Shapiro DB, Osterman AL, Chu-Andrews J. Carpal tunnel syndrome, tarsal tunnel syndrome, and double crush syndrome, and their relationship to trauma. In: Simon WH, Ehrlick GE, eds. Medicolegal consequences of trauma. New York: Marcel Dekker, 1993;215-253.
35. Yu J, Bendler EM, Mentari A. Neurological disorders associated with carpal tunnel syndrome. *Electromyogr Clin Neurophysiol* 1979;19:27-32.
36. Nakano KK, Lundergan C, Okihiro MM. Anterior interosseous nerve syndromes. *Arch Neurol* 1977;34:477-480.
37. Hirsh LF, Thanki A. Ulnar nerve entrapment at the elbow. *Postgrad Med* 1985;77:211-215.
38. Niakan E, Harati Y, Ashizawa T. Double-crush syndrome in patients with spasmodic torticollis. *Neurology* 1988;38:204-205.
39. Lundborg G. Nerve injury and repair. Edinburgh: Churchill-Livingstone, 1988.
40. Mackinnon SE. Double and multiple "crush" syndromes. *Hand Clin* 1992;8:369-390.
41. Dyro FM. Peripheral entrapments following brachial plexus lesions. *Electromyogr Clin Neurophysiol* 1983;23:251-256.
42. Reddy MP. Nerve entrapment syndromes in the upper extremity contralateral to amputation. *Arch Phys Med Rehabil* 1984;65:24-26.
43. Crane CR. Carpal tunnel syndrome associated with thoracic

- outlet conduction slowing. *Electromyogr Clin Neurophysiol* 1973;13:142-143.
47. Novak CB, Mackinnon SE, Patterson GA. Evaluation of patients with thoracic outlet syndrome. *J Hand Surg Am* 1993;18:292-299.
  48. Novak CB, Collins ED, Mackinnon SE. Outcome following conservative management of thoracic outlet syndrome. *J Hand Surg Am* 1995;20:542-548.
  49. Sucher BM. Palpatory diagnosis and manipulative management of carpal tunnel syndrome: part 2. "Double crush" and thoracic outlet syndrome. *J Am Osteopath Assoc* 1995;95:471-479.
  50. Williams TH, Carpenter NH. Surgical treatment of the thoracic outlet compression syndrome. *Arch Surg* 1978;113:850-852.
  51. Wood VE, Biondi J. Double-crush nerve compression in thoracic-outlet syndrome. *J Bone Joint Surg Am* 1990;72:85-88.
  52. Wood VE, Twito R, Verska JM. Thoracic outlet syndrome. The results of first rib resection in 100 patients. *Orthop Clin North Am* 1988;19:131-146.
  53. Dixon JA. Double-crush syndrome: thoracic outlet and pronator syndrome in combination. *Osteopath Med* 1993;7:42-51.
  54. Leffert RD. Anterior submuscular transportation of the ulnar nerves by the Learmonth technique. *J Hand Surg* 1982;7:147-155.
  55. Leffert RD, Goldner JL. Ulnar neuropathy and thoracic outlet syndrome. *Orthop Consult* 1989;11:1-9.
  56. Morin JE, Long R, Elleker MG, Eisen AA, Wylands E, Ralphs-Thibodeau S. Upper extremity neuropathies following median sternotomy. *Ann Thorac Surg* 1982;34:181-185.
  57. Putters JLM, Kaulesar-Sukul DMKS, Johannes EJ. Bilateral thoracic outlet syndrome with bilateral radial tunnel syndrome: a double-crush phenomenon. *Arch Orthop Trauma Surg* 1992;111:242-243.
  58. Ferrante MA, Wilbourn AJ. The utility of various upper extremity sensory nerve conduction responses in assessing brachial plexopathies. *Muscle Nerve* 1995;18:879-889.
  59. Gainor BJ. The pronator compression test revisited. A forgotten physical sign. *Orthop Rev* 1990;19:888-892.
  60. Zamora JL, Rose JE, Rosario V, Noon GP. Double entrapment of the median nerve in association with PTFE hemodialysis loop grafts. *South Med J* 1986;79:638-640.
  61. Jones NF, Ming NL. Persistent median artery as a cause of pronator syndrome. *J Hand Surg Am* 1988;130:728-732.
  62. Dahlin LB, Lundborg G. The neurone and its response to peripheral nerve compression. *J Hand Surg Br* 1990;15:5-10.
  63. Sponseller PD, Engber WD. Double-entrapment radial tunnel syndrome. *J Hand Surg* 1983;8:420-423.
  64. Idusuyi OB, Morrey BF. Peroneal nerve palsy after total knee arthroplasty. *J Bone Joint Surg Am* 1996;78:177-184.
  65. Chodoroff B, Ball RD. Lumbosacral radiculopathy, reflex sympathetic dystrophy and tarsal tunnel syndrome: an unusual presentation. *Arch Phys Med Rehabil* 1985;66:185-187.
  66. Augustyn P, Vanneste J. The tarsal tunnel syndrome after a proximal lesion. *J Neurol Neurosurg Psychiatry* 1992;55:65-67.
  67. Wilbourn AJ, Porter J. Thoracic outlet syndromes. *Spine: State of the Art Reviews* 1988;2:597-626.
  68. Idler RS. Persistence of symptoms after surgical release of compressive neuropathies and subsequent management. *Orthop Clin North Am* 1996;27:409-416.
  69. Crandall RE, Weeks PM. Multiple nerve dysfunction after carpal tunnel release. *J Hand Surg Am* 1988;13:584-589.
  70. Lishman WA, Russell WR. The brachial neuropathies. *Lancet* 1961;2:941-947.
  71. McLellan DL. Longitudinal sliding of median nerve during hand movements: a contributory factor in entrapment neuropathy? *Lancet* 1975;1:633-634.
  72. Murray-Leslie F, Wright V. Carpal tunnel syndrome, humeral epicondylitis, and the cervical spine: a study of clinical and dimensional relations. *BMJ* 1976;5:1439-1442.
  73. Crymble B. Brachial neuralgia and the carpal tunnel syndrome. *Br Med J* 1968;3:470-471.
  74. Dellon AL, Mackinnon SE. Radial sensory nerve entrapment in forearm. *J Hand Surg Am* 1986;11:199-205.
  75. Simpson RL, Fern SA. Multiple compression neuropathies and the double-crush syndrome. *Orthop Clin North Am* 1996;27:381-388.
  76. Askin SR, Hadler NM. [letter]. *J Bone Joint Surg Am* 1991;73:629.
  77. Wilbourn AJ, Breuer AC. The double crush syndrome: a reappraisal. *Neurology* 1986;36(suppl 1):234-235.
  78. Payan J. Editorial: the carpal tunnel syndrome: can we do better? *J Hand Surg Br* 1988;13:365-367.
  79. Carroll RE, Hurst LC. The relationship of thoracic outlet syndrome and carpal tunnel syndrome. *Clin Orthop* 1982;164:149-153.
  80. Clemente CD, ed. *Gray's anatomy of the human body*. 30th ed. Philadelphia: Lea & Febiger, 1985.
  81. Bonney G, Gilliatt RW. Sensory nerve conduction after traction lesion of the brachial plexus. *Proc R Soc Med* 1958;51:365-367 (Clin Sec).
  82. Dumitru D. *Electrodiagnostic medicine*. Philadelphia: Hanley & Belfus, 1995.
  83. Ochs S, Erdman J, Jerald RA, McAdoo V. Routing of transported materials in the dorsal root and nerve fiber branches of the dorsal root ganglion. *J Neurobiol* 1978;9:465-481.
  84. Ochs S. Rate of fast axoplasmic transport in mammalian nerve fibers. *J Physiol* 1972;227:627-645.
  85. Magnotta JA, Wilbourn AJ. Ulnar neuropathy at the elbow: the electrodiagnostic findings in 240 limbs of 200 patients. *Muscle Nerve* 1994;17:1110.
  86. Stevens JC. AAEE minimonograph #26: the electrodiagnosis of carpal tunnel syndrome. *Muscle Nerve* 1987;10:99-113.
  87. Morgan G, Wilbourn AJ. Cervical radiculopathy and coexisting carpal tunnel syndrome: a double crush syndrome? (submitted for publication).