Multifocal Neuropathy: Expanding the Scope of Double Crush Syndrome

Brian H Cohen, MD,* Michael P. Gaspar, MD,† Alan H Daniels, MD,*
Edward Akelman, MD,* Patrick M. Kane, MD†

Double crush syndrome (DCS), as it is classically defined, is a clinical condition composed of neurological dysfunction due to compressive pathology at multiple sites along a single peripheral nerve. The traditional definition of DCS is narrow in scope because many systemic pathologic processes, such as diabetes mellitus, drug-induced neuropathy, vascular disease and autoimmune neuronal damage, can have deleterious effects on nerve function. Multifocal neuropathy is a more appropriate term describing the multiple etiologies (including compressive lesions) that may synergistically contribute to nerve dysfunction and clinical symptoms. This paper examines the history of DCS and multifocal neuropathy, including the epidemiology and pathophysiology in addition to principles of evaluation and management. *(J Hand Surg Am. 2016;■(■):■−■. Copyright © 2016 by the American Society for Surgery of the Hand. All rights reserved.)*

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Peripheral neuropathies are among the most common conditions encountered by orthopedic, spine, hand, and neurosurgeons in the United States and worldwide.[1,2] Although compression neuropathies, such as carpal and cubital tunnel syndrome, compose a significant proportion of these cases, the full spectrum of related conditions is far more encompassing. When multiple sites or disease processes contribute to a single neuropathy, the underlying etiology can become increasingly difficult to elucidate. Historically, the condition in which multiple sites of compression are found on the same peripheral nerve has been termed double crush syndrome (DCS). This phrase was originally coined in 1973 by Upton and McComas[3] as a means of explaining how one site of injury on a nerve made that nerve more susceptible to injury at another location.

Although the mechanism behind DCS was originally well accepted, recent years have seen an increase in the volume of literature disputing prior explanations of DCS and even the term itself.[4–7] In particular, many authors now feel that focusing the pathophysiology of DCS solely on mechanical crush or compression is too limiting and perhaps even misleading.[7] In this review, we aim to revisit the background of DCS, including its epidemiology and pathophysiology, and principles in its evaluation and management. In addition, our goal is to propose a new term, multifocal neuropathy (MFN), which we believe will address the shortcomings of classic DCS when used to explain these complex conditions.

EPIDEMIOLOGY

Because there are no standardized or validated criteria to define or diagnose DCS, no true consensus exists regarding its prevalence or general epidemiology.

*From the *Department of Orthopedics, The Warren Alpert Medical School of Brown University, Providence, RI; and the †The Philadelphia Hand Center, PC, Thomas Jefferson University, Philadelphia, PA.*

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Corresponding author: Brian H. Cohen, 593 Eddy St., Providence, RI 02903; e-mail: bharriscohen@gmail.com.

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The most widely studied association is that between carpal tunnel syndrome (CTS) and cervical radiculopathy (CR).[8–12] However, even among this subset of studies, reported incidences of concomitant CTS and CR vary widely from less than 10% to greater than 70%.[3,9] Furthermore, the relative roles of patient symptomatology, physical examination findings, electrodiagnostic testing, and imaging in making a definitive diagnosis of DCS are unclear and vary from study to study.[9,13] For example, Morgan and Wilbourn[9] reviewed over 12,000 patients using rigid clinical, electrodiagnostic, and anatomical criteria to determine a true incidence of DCS, for which they found that the incidence of concomitant CTS or cubital tunnel syndrome with CR was less than 1%. This is in stark contrast to the original study by Upton and McCombs,[3] who reported a 76% incidence of concomitant CTS and CR.

Likely owing to the variability in what is defined as DCS, risk factors for developing the condition are also debated. Although it would seem reasonable that risk factors for the individual processes present in DCS would also predispose one to DCS itself, this relationship does not always hold true. Although females are generally at higher risk for developing CTS, sex distribution of DCS varies between studies.[12,14] In fact, in 2 separate studies from the same group, female sex was found to be an independent risk factor for CTS, whereas male sex was found to be an independent risk factor for DCS.[14,15] These reports highlight the need for additional study regarding the risk factors for DCS, with the caveat that, without establishing more objective diagnostic criteria for DCS, future studies would likely be subject to the same inconsistencies.

PATHOPHYSIOLOGY

The underlying pathophysiology of DCS is also widely debated. When originally described by Upton and McCombs,[3] the authors theorized that compression at one location on a nerve's axon would predispose that same axon to injury elsewhere. They reasoned that this increased susceptibility to injury resulted from disrupted bidirectional transport of essential nutrients along the axon. Unable to obtain and utilize nutrients where necessary, the nerve would gradually undergo morphological and functional changes, ultimately manifested by various symptoms seen in DCS.[3] This has since been supported extensively, with some authors adding that more proximal lesions (closer to the cell body) have a greater effect on nerve function.[16–20] Although evidence for disruption of axonic flow due to compression is extensive, resultant clinical effect remains a topic of significant debate.[3,4]

Regardless of the true underlying pathological processes involved, it has become apparent that the phrase "double crush" may itself be somewhat misleading. Upton and McComas[3] themselves acknowledged this shortcoming, as double would not take into account conditions in which 3 or more sites of a given nerve are affected. In addition, crush, which implies compression, would not take into account other mechanical stresses on a nerve that may produce the same adverse outcome, such as stretch.[7] More significantly, we feel that crush also limits the scope of the disease to one that is purely mechanical, whereas multiple medical and pharmacological factors are also likely to contribute. Thus, we feel it necessary to expand the term to multifocal neuropathy (MFN) to emphasize 2 caveats to the original description of DCS: (1) although mechanical compression may play a role in the disease process, a complex interplay among mechanical, systemic, pharmacological, and even environmental factors may also be contributory, and (2) although there may be one or more distinct location(s) of injury that predispose a nerve to injury elsewhere, global or systemic conditions may play an equal, or even greater, role in contributing to the clinical sequelae (Fig. 1). The list of such contributing conditions is vast and includes endocrine, nutritional, metabolic, genetic, iatrogenic, anatomical, infectious, and systemic pathologies.[7,21–27]

CLINICAL PRESENTATION AND PHYSICAL EXAMINATION

As one would expect, clinical features of MFN/DCS are highly variable and largely dependent on numerous factors including which particular nerves are affected, where they are affected, the manner in which they are affected (compression vs stretch), and contributing underlying comorbidities. Again, much of the previous literature is focused on the DCS occurring in the upper extremity, particularly in patients with concomitant CR and CTS. It is important to note, however, that the potential combinations and sites of nerve compression are vast and involve both the upper and the lower extremities. In addition, pathology can occur at any location along the course of a nerve and, potentially, at more than 2 locations.

Using the classic scenario of DCS due to CR with CTS, Osterman[8] reported key findings that may differentiate between DCS and isolated CTS patients.