
Mark A. Ferrante, MD¹ and Nicole D. Ferrante, MD²

¹Professor, Department of Neurology, Co-Director, Neurophysiology Fellowship, Assistant Director, Residency Training Program, University of Tennessee Health Science Center and Section Chief, Neurophysiology, Department of Neurology, VAMC, Memphis, Tennessee

²Department of Internal Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

Reprint Requests

6614 Heronswood Cove

Memphis, TN 38119

Abbreviations: AHC, anterior horn cell; AP, action potential; APR, anterior primary rami; A-TOS, arterial thoracic outlet syndrome; CT, computerized tomography; CTS, carpal tunnel syndrome; DRG, dorsal root ganglion; EDX, electrodiagnostic; EMG, electromyography; FTR, first thoracic rib; LABC, lateral antebrachial cutaneous; MABC, medial antebrachial cutaneous; Med-D1, median sensory response recording from the thumb; Med-D2, median sensory response recording from the index finger; MR, magnetic resonance; MRI, magnetic resonance imaging; MRN, magnetic resonance neurography; MUAP, motor unit action potential; NCS, nerve conduction study(ies); PNS, peripheral nervous system; SR-DH, superficial radial sensory response recording dorsum of hand; TN-TOS, true neurogenic thoracic outlet syndrome; TOS,
The Thoracic Outlet Syndromes, Part 1

thoracic outlet syndrome; Uln-D5, ulnar sensory response recording from the little finger; V-TOS, venous thoracic outlet syndrome.

**Key Words:** cervical rib, fibrous band, rib and band syndrome, thoracic outlet, thoracic outlet syndrome, brachial plexus, lower trunk, subclavian artery, subclavian vein

**Acknowledgement:** The author wishes to thank Dr. Asa J. Wilbourn (deceased) for bequeathing me his collection of publications on the various thoracic outlet syndromes, including hundreds of articles, fully translated foreign articles, and difficult to obtain textbook chapters. This paper underwent peer review by the AANEM Monograph Review and Development/Issues & Opinions Committee and review by the Muscle & Nerve editor, but did not undergo additional peer review via the Muscle & Nerve editorial process. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. None of the authors has any conflict of interest to disclose.

**Running title:** The Thoracic Outlet Syndromes, Part 1
ABSTRACT: The thoracic outlet syndromes (TOSs) are a group of etiologically and clinically distinct disorders with 1 feature in common: compression of 1 or more neurovascular elements as they traverse the thoracic outlet. The medical literature reflects 5 TOSs: arterial, venous, traumatic neurovascular, true neurogenic, and disputed. Of these, the first 4 demonstrate all of the features expected of a syndrome, whereas disputed TOS does not, causing many experts to doubt its existence altogether. Thus, some categorize disputed TOS as a cervicoscapular pain syndrome rather than as a type of TOS. To better understand these disorders, their distinctions, and the reasoning underlying the categorical change of disputed TOS from a form of TOS to a cervicoscapular pain syndrome, a thorough understanding of the pertinent anatomy, pathology, pathophysiology, and the electrodiagnostic manifestations of their pathophysiologies is required. This review of the TOSs is provided in two parts. The first part discusses information pertinent to all 5 TOSs and reviews true neurogenic TOS. The second part will review the other 4 TOSs.
INTRODUCTION

The thoracic outlet syndromes (TOSs) are a diverse group of etiologically and clinically distinct disorders with 1 feature in common, namely, the compression of 1 or more neurovascular elements as they traverse the thoracic outlet (see Figure 1).¹ Previous terms for the various TOSs reflected either the anatomic structure suspected to be responsible for the compression or the particular maneuver that precipitated the symptoms. These terms included “cervical rib and band syndrome” (classic TOS), “scalenus anticus syndrome,” “costoclavicular syndrome,” “pectoralis minor syndrome,” “hyperabduction syndrome,” and many others. As these disorders became better understood, these terms were either excluded or modified. The current medical literature considers 5 entities as TOSs: arterial TOS (A-TOS), venous TOS (V-TOS), traumatic neurovascular TOS, true neurogenic TOS (TN-TOS), and disputed TOS.¹² Of these 5 disorders, the first 4 demonstrate all of the features expected of a syndrome, including: (1) an anatomical abnormality, (2) a pathogenesis related to that abnormality, (3) a constellation of clinical features related to the abnormality, (4) a method of testing that identifies the abnormality, and (5) a treatment that addresses the abnormality. Conversely, disputed TOS lacks a consistent anatomical abnormality, a recognized pathogenesis, consistent clinical features, a reliable method of testing, and a standard treatment. Consequently, many experts doubt its existence altogether. Although disputed TOS is better considered a cervicoscapular pain syndrome, it will be referred to as disputed TOS.

To better understand these disorders and their distinctions, a thorough understanding of the pertinent anatomy, pathology, pathophysiology, and, especially, the electrodiagnostic (EDX) manifestations of the various pathophysiologies associated with nerve fiber disruption is
required. This understanding will: (1) permit lesion localization to the lower plexus, (2) generate an understanding of the different EDX manifestations of focal demyelination and axon loss, and (3) support the belief that disputed TOS is a pain syndrome. Physicians without this understanding will have an incomplete and inaccurate understanding of these disorders, particularly disputed TOS, that may have a negative impact on clinical management and generate unwanted medical and legal repercussions related to misdiagnosis, improper treatment, and increased patient morbidity and mortality.

Because of the broad scope of this topic, this review is presented in two parts. This first part introduces the background information necessary for a complete understanding of the 5 thoracic outlets syndromes and reviews the type of TOS most important to neurologists: true neurogenic TOS. The second part reviews the other 4 types of TOS.

PERTINENT ANATOMIC, PATHOLOGIC, PATHOPHYSIOLOGIC, ELECTRODIAGNOSTIC, AND PROGNOSTIC INFORMATION

Anatomy. The Thoracic Cage. The thoracic cage, or rib cage, is composed of the sternum, 12 thoracic vertebrae, 12 rib pairs, and various musculoskeletal elements joining these structures. The opening at the top of the rib cage, the “superior thoracic aperture” or “thoracic inlet,” is bounded by the first thoracic vertebra, the first pair of thoracic ribs, the costal cartilage of the first rib, and the superior edge of the manubrium. The opening at the bottom, where the diaphragm attaches, is termed the “inferior thoracic aperture” or “thoracic outlet.”

The First Thoracic Ribs. Because the superior thoracic aperture is smaller than the inferior one, the first thoracic ribs (FTRs) are the shortest and most curved rib pair. Each consists
The head of the FTR attaches to the T1 vertebral body. Also, a tubercle at the junction of the neck and body of the rib attaches to the T1 transverse process. Anterior to this tubercle, the middle scalene muscle, the first digitation of the serratus anterior muscle, and the musculature of the first intercostal space attach. More anteriorly, a small bony ridge separates 2 shallow grooves, termed the “anterior groove” and the “posterior groove.” Medially, this ridge forms the scalene tubercle. The anterior scalene muscle, the subclavius muscle, and the costoclavicular ligaments attach to this tubercle. The subclavian artery traverses the posterior groove (between the anterior and middle scalene muscle attachment sites) just anterior to the lower trunk of the brachial plexus, whereas the subclavian vein traverses the anterior groove (anterior to the anterior scalene muscle attachment site) (Figure 2). Anomalous FTRs occur and are observed equally among males and females.  

**Cervical Ribs.** During early development, the ossified lateral costal element of the C7 vertebral body is reabsorbed. When this does not occur, either an elongated transverse process or a C7 rib results. Historically, cervical ribs were first described during human dissections by Galen and Vesalius around 150 AD. Hunald, a German anatomist, authored a detailed study of cervical ribs in the 18th century and, in 1869, Gruber classified them based on their length and whether or not they contacted the manubrium. In 1895, concomitant with the advent of radiographs, cervical ribs were increasingly recognized. Their prevalence ranges from 0.5% to 2% and they are traditionally considered to be more frequently left-sided and more common among females. Recently, however, a study of stillborn fetuses showed an equal sex distribution and unilaterality more common on the right. The incidence of C7 bony anomalies may vary among different populations. In Saudi Arabia, a 3.4% prevalence of cervical ribs and a 23% prevalence of elongated C7 transverse processes have been reported. The majority of
individuals with cervical ribs are asymptomatic and, consequently, the identification of cervical ribs by routine chest radiograph typically represents an incidental finding. When symptomatic, the size and type of the C7 bony anomaly correlates, to some degree, with the TOS type. For example, the cervical ribs associated with TN-TOS tend to be incomplete (not connecting to the manubrium), of intermediate length, and connected to the FTR via a fibrous band (less commonly, via cartilage or bone), whereas those responsible for the subclavian artery compression associated with A-TOS tend to be larger.\textsuperscript{1,12}

**The Scalene Muscles.** The scalene muscles (anterior, middle, and posterior) originate from the transverse processes of the C2 through C7 vertebrae and insert onto the first and second thoracic ribs. The term “scalene” (Greek for uneven) reflects the different lengths of these muscles. Of these 3 muscle pairs, only the anterior and middle scalene muscles are pertinent. The anterior scalene (scalenus anterior, scalenus anticus) muscles are located beneath the sternocleidomastoid muscles and are innervated by motor axons emanating from the C5 and C6 anterior primary rami (APR). Each originates from the C3-C6 transverse processes and inserts into the scalene tubercle of the first rib (and the upper aspect of the second rib). The middle scalene muscles (scalenus medius) are the largest and longest. They arise from the C2-C7 transverse processes and insert into the first rib, between the scalene tubercle and the posterior groove (Figure 2).

**The Lower Plexus.** In the anatomical position, the brachial plexus can be divided into 3 smaller plexuses: the supraclavicular plexus (C5-T1 roots; upper, middle, and lower trunks), the retroclavicular plexus (3 anterior divisions; 3 posterior divisions), and the infraclavicular plexus (lateral, posterior, and medial cords; musculocutaneous, axillary, median, radial, and ulnar
terminal nerves). The supraclavicular plexus also consists of 3 parts: the upper plexus (upper trunk; C5 root; C6 root), middle plexus (middle trunk; C7 root), and lower plexus (lower trunk; C8 root; T1 root). This simple approach has considerable clinical utility because the incidence, severity, prognosis, and lesion type vary among these regions. It also facilitates communication among physicians when precise localization is unclear, such as when non-neural injuries delay clinical examination, when examination is limited by factors such as pain or mental status changes, and when diagnostic testing has not yet been performed. For example, C5-6–distribution weakness following a supraclavicular fossa penetration injury can be localized to the upper plexus before committing to a more specific element such as the upper trunk, C5 root, or C6 root).

The motor and sensory axons contained within a peripheral nervous system (PNS) element dictate its muscle (motor) and cutaneous (sensory) domains. The muscle domains of the various brachial plexus elements are easily deduced from published studies defining the root and peripheral nerve innervations of those muscles that receive motor axons that traverse the brachial plexus. For example, the first dorsal interosseous muscle is a C8-T1 ulnar nerve-innervated muscle. Therefore, the motor axons innervating this muscle must traverse the C8 and T1 roots, the lower trunk, the medial cord, and the ulnar nerve. Accordingly, the first dorsal interosseous muscle belongs to the muscle domain of all of these elements. A more cumbersome approach is to begin with the muscle domains of the roots (the myotomes) and then add or subtract muscles as the different brachial plexus elements fuse or separate from each other. For example, because the C8 and T1 roots fuse to form the lower trunk without giving off any branches, the muscle domain of the lower trunk is equivalent to the summed muscle domains of the C8 and T1 roots (Table 1).
This same approach can be used to define the cutaneous domains of PNS elements. Thus, the cutaneous domain of the lower plexus includes the summed cutaneous domains of the ulnar, medial antebrachial cutaneous, and medial brachial cutaneous nerves. In approximately 20% of individuals, it also includes the median nerve-innervated skin of the middle finger (Table 1).  

**The Thoracic Outlet.** Although the term “thoracic outlet syndrome” is a misnomer (the superior opening of the thoracic cage is the thoracic inlet), to avoid confusion, it will be used throughout this manuscript. Anatomically, it extends from the base of the neck to the axilla and contains 3 smaller regions: (1) the interscalene (or scalene) triangle (the tissue volume demarcated by the anterior scalene muscle anteriorly, the middle scalene muscle posteriorly, and the FTR inferiorly; see Figure 2), (2) the costoclavicular space (bordered by the FTR inferiorly, the clavicle superiorly, and the anterior scalene muscle at its insertion site posteriorly, and (3) the subclavoid (or retropectoralis minor) space (the space located beneath the pectoralis minor tendon). The subclavius muscle and tendon are located medial to the costoclavicular space, just posterior to the intersection of the clavicle and the FTR. The neurovascular supply to the shoulder and upper extremity traverses the thoracic outlet, and is comprised of the brachial plexus and the subclavian and axillary arteries and veins (the axillary vessels are distal continuations of the subclavian vessels). When clinical features of compressive pathology involve at least 1 of these elements as it traverses the thoracic outlet, the term TOS is applicable. Examples of compressive pathology include C7 vertebral body anomalies (C7 rib or elongated C7 transverse process, typically with a taut fibrous band connecting the bony anomaly to the FTR), scalene muscle or tendon hypertrophy, and other structural abnormalities. The specific neurovascular element compressed dictates the particular type of TOS, the resultant clinical features, the diagnostic evaluation, and the proper treatment (except for disputed TOS).
Nerve Fiber Pathology and Pathophysiology. Despite the large number of mechanisms by which nerve fibers can be injured, the resultant pathology is limited to myelin damage (no distant effects) or axon damage (distant effects related to Wallerian degeneration of the distal stump). These 2 pathologies generate 3 pathophysiologies. With focal demyelination, depending on the severity of disruption, action potentials (Aps) are either able traverse the demyelinated segment, albeit at a slower rate (demyelinating conduction slowing), or unable to traverse it (demyelinating conduction block). With axon disruption, the distal stump degenerates (conduction failure).\textsuperscript{17}

EDX Manifestations. EDX testing consists of 2 parts: nerve conduction studies (NCSs), including sensory NCSs and motor NCSs, and needle electromyography (EMG). In order to fully appreciate the EDX manifestations of TN-TOS and the shortcomings of the EDX techniques purported to identify disputed TOS, it imperative to understand the EDX manifestations of each pathophysiology.

Focal Demyelination. This finding is only appreciable by NCS when the stimulating and recording surface electrodes straddle the lesion. With demyelinating conduction slowing, the nerve fiber action potential (AP) propagation speed is decreased. This may be uniform (when the stimulated fibers are affected to similar degrees) or nonuniform (when affected to varying degrees). Consequently, with uniform demyelinating conduction slowing, the waveform is delayed but the morphology is unaffected. With nonuniform demyelinating conduction slowing, however, the morphology of the waveform is dispersed, the amplitude is reduced, and the negative area under the curve is negligibly reduced. Because of their small amplitudes (\textmu V range), short durations (around 2 msec), and wid range of conduction velocities (25 m/s between
fastest and slowest fibers), sensory responses are susceptible to physiologic dispersion and, hence, cannot be used to screen long nerve segments for focal demyelination. Conversely, because of their large amplitudes (mV range), long durations (10 msec), and narrow range of conduction velocities (12 m/s), motor responses have much greater resistance to physiological dispersion and, hence, are able to assess long nerve segments for focal demyelination. With demyelinating conduction slowing, needle EMG is normal. Clinically, because all of the APs reach the target organ (muscle fiber; sensory receptor) these lesions are either asymptomatic or associated with positive symptoms (episodic paresthesias). Symptom resolution follows remyelination.

With demyelinating conduction block, the APs are unable to traverse the lesion site. Hence, the amplitude of the motor response and the negative area under the waveform curve are reduced with nerve stimulation proximal to the lesion and are normal with nerve stimulation distal to the lesion. The difference between the proximal and distal responses estimates the percentage of blocked nerve fibers. The duration of the negative phase is unchanged or reduced, depending on the conduction speeds of the involved fibers. Needle EMG shows rapid firing of a reduced number of motor unit action potentials (neurogenic recruitment) when the lesion is moderate to severe in degree. The observed MUAPs are normal in morphology. Clinically, negative symptoms (weakness and numbness) result because the APs do not reach their target organs. Because the axon is intact, muscle atrophy does not occur.

**Axon Degeneration.** Because axon disruption leads to degeneration of the nerve segments distal to the disruption, the amplitude and negative area under the curve values are reduced regardless of the stimulation site. With proximal stimulation, the APs reach the lesion...
site, but cannot conduct through it, whereas with distal stimulation, APs cannot be generated from the degenerated segments. Thus, NCS identify axon disruption located between the stimulating and recording electrodes and proximal to them. Because neuronopathies result in axon degeneration, they are also identified.

Prior to Wallerian degeneration, the distal segment remains capable of generating and transmitting APs. Therefore, the distal response is normal and the proximal response is reduced, similar to the pattern observed with demyelinating conduction block. This can be termed “transient axonal conduction block.” Because neuromuscular junction degeneration precedes nerve fiber degeneration, the motor responses (which assess neuromuscular junction transmission) are affected before the sensory responses. In general, the motor responses begin to diminish in size on day 3 after then insult and reach their nadir by day 7, whereas sensory response diminution begins on day 6 and is complete by day 10.19 Because axon degeneration results in muscle fiber denervation, fibrillation potentials are noted on needle EMG. In general, these potentials do not appear until 21 days after axon disruption (up to 5 weeks in some individuals at some locations). To avoid making inaccurate conclusions, the temporal relationship between symptom onset and the EDX study must be known.

The motor unit is defined as one anterior horn cell (AHC) and all of the muscle fibers it innervates. Thus, MUAPs are compound electrical potentials composed of the individual muscle fiber APs of the unit. With motor axon disruption, the total number of MUAPs decreases and, thus, less contractile force is generable. Normally, as contractile force increases, more and more motor units are recruited (spatial recruitment) at faster and faster rates (temporal recruitment). Spatial and temporal recruitment are concordant. With axon loss, however, spatial recruitment is
reduced and temporal recruitment is normal. Thus, the monitor shows a reduced number of MUAPs firing at rates faster than those normally discernible. Importantly, the faster rates are not abnormal; it is their discernibility that is abnormal. Normally, these higher rates would not discernible because of the normal MUAP overlap that occurs with increasing spatial recruitment. This discordance between spatial and temporal recruitment is termed neurogenic MUAP recruitment. Neurogenic MUAP recruitment only occurs in 2 settings: (1) focal demyelinating conduction block and (2) axon degeneration. With poor effort for any reason (pain; malingering; hysteria/conversion), the relationship between spatial and temporal recruitment is normal (both are low in the setting of reduced effort). Following axon loss (2-3 months or so), reinnervation via collateral sprouting occurs, increasing the innervation ratio (the number of muscle fibers innervated per AHC) of the adopting AHC and, hence, the size of its MUAP. The presence of reinnervation by collateral sprouting is best appreciated by measuring the duration of the MUAP rather than its amplitude; the latter is typically normal unless the process is severe in degree and very slowly progressive.

Nerve Lesion Prognostication. The prognosis for neural recovery reflects the likelihood of reinnervation, which occurs in 2 ways: proximodistal axonal regrowth and distal axon sprouting from unaffected axons (collateral sprouting). The former is time dependent, whereas the latter is dependent on lesion completeness. Because the rate of axon regrowth is typically 1 inch per month and because denervated muscle fibers degenerate within 20-24 months, denervated muscle fibers located more than 20-24 inches from the lesion site typically cannot recover by this mechanism. For example, the distal forearm and hand muscle denervation associated with lower plexus lesions cannot recover via proximodistal axonal regrowth and, hence, depends on reinnervation via collateral sprouting. Because collateral sprouting requires unaffected...
intramuscular axons from which to sprout, it only occurs with incomplete lesions. With complete lower plexus lesions, neither mechanism of reinnervation is available. Because collateral sprouting usually occurs within 2-3 months or so, any neurological abnormalities related to lower plexus involvement that persist beyond 3 months are likely permanent without surgical intervention.

**TRUE NEUROGENIC TOS**

TN-TOS, which was first reported in 1903 by Thomas and Cushing, is also termed “classic TOS” and “cervical rib and band syndrome.” The latter term reflects the taut fibrous band that extends from the FTR to the C7 rib and that angulates and stretches the lower plexus (discussed below).

**Epidemiology.** Although neurogenic TOS is frequently reported to be more common than vascular TOS and, in 1 series accounted for 95% of TOS patients, this reflects the lumping together of TN-TOS and disputed TOS. Indeed, in that series, disputed TOS represented 99% of the neurogenic TOS patients. This lumping typically occurs in the surgical literature. When disputed TOS is excluded, V-TOS is the most common type of TOS and TN-TOS is rare, with a prevalence of about 1 per million individuals.

Most individuals with TN-TOS are young to middle-aged adults at presentation, the majority of whom are women. In the largest series of surgically-verified TN-TOS patients (n=32), the mean age was 40.7 years (range 17-77 years), symptoms involved the dominant limb in 81% (26 of 32), and women accounted for 94% (30 of 32) of the patients. The reason for the
greater incidence among women is unclear but some of this inequality may reflect their higher incidence of cervical ribs. Importantly, the presence of a cervical rib is not synonymous with TN-TOS. Statistically, based on a cervical rib prevalence of 0.5-2%\(^7,9,10\) and a TN-TOS prevalence of 1 per million,\(^26\) the ratio of cervical ribs to TN-TOS is 5000-20,000:1. Thus, at most, 1 per 5000 individuals with a cervical rib will have TN-TOS. Consequently, when individuals with nonspecific upper extremity symptoms are found to have a cervical rib during their evaluation, it most likely is incidental. However, when concomitant clinical and EDX features indicative of C8 and T1 nerve fiber disruption are present (discussed below), it is much more likely that the cervical rib is pathogenic.

**Pathogenesis and Pathophysiology.** With TN-TOS, the lower plexus is stretched and angulated superiorly, typically by an inferiorly located fibrous band that extends from the FTR to a C7 rib or, less commonly, to an abnormally elongated C7 transverse process.\(^1\) Although the majority of patients with TN-TOS have a C7 bony anomaly as the underlying cause, this is not always the case. In our series of 32 patients, although 100% had a surgically-verified fibrous band displacing the lower plexus upward, only 79% (23 of 29) had a C7 bony anomaly on the symptomatic side (bilateral bony anomalies were noted in two-thirds).\(^25\) In 1995, Katirji and Hardy reported a case of TN-TOS in a competitive long distance freestyle and butterfly swimmer who also lacked a C7 bony anomaly.\(^27\) In that patient, supraclavicular exploration identified thickening of the lower trunk and a hypertrophied anterior scalene muscle containing a fibrous band. The muscle hypertrophy was postulated to be secondary to the particular swim stroke utilized by freestyle swimmers. Importantly, even when a C7 bony anomaly is not visualized, a fibrous band compressing the lower plexus is typical.
Conversely, among surgical reports, the incidence of bony anomalies is much lower.\textsuperscript{28,29} In 1 surgical series, the incidence of bony anomalies was only 4.6%.\textsuperscript{30} As previously stated, this reflects the lumping of TN-TOS with disputed TOS and the lack of a confirmatory diagnostic test for disputed TOS.

\textbf{Clinical Features.} Anatomically, the lower plexus consists of the lower trunk distally and the C8 and T1 roots proximally.\textsuperscript{14} The fibrous band typically contacts the lower plexus at the distal APR level, just prior to the proximal aspect of the lower trunk.\textsuperscript{26} Because the T1 APR lies inferior to the C8 APR, the T1 APR is stretched more than the C8 APR. Intraoperatively, the T1 root appears obviously more angulated, more erythematous, and more edematous than the C8 root.

Accordingly, the sensory and motor axons of the T1 APR sustain more severe injury than those composing the C8 APR.\textsuperscript{24,26} This same pattern is observed with fibrous band contact at the proximal aspect of the lower trunk because the T1 axons are more inferior than the C8 axons. This T1 axon > C8 axon involvement evident clinically and electrodiagnostically.\textsuperscript{1,16}

Because the fibrous band involves the lower plexus, the motor and sensory abnormalities lie within the muscle and cutaneous domains of the C8 and T1 roots (Table 1). Regarding the motor features, because of the T1 > C8 pattern of motor axon involvement and because the muscles of the thenar eminence are innervated primarily by motor axons derived from the T1 spinal cord segment, these muscles are affected more than the other involved muscles (Figure 3).\textsuperscript{1,6,26,31-33} Thorburn first reported this pattern of muscle involvement over a century ago.\textsuperscript{24} Because the natural history of TN-TOS is slow progression, muscle fiber reinnervation (via collateral sprouting) is able to keep pace with the slow rate of muscle fiber denervation. Consequently, most patients do not recognize the motor involvement in its earlier stages and,
hence, typically do not seek medical attention until the motor features are quite advanced. Invariably, the motor abnormalities are much more pronounced than the sensory abnormalities. In general, most patients present with intrinsic hand muscle weakness and wasting that is most pronounced in the muscles of the thenar eminence. Not infrequently, wasting is brought to their attention by a colleague or their primary care provider. Other common motor complaints include progressive inability to use the hand and loss of dexterity. In our series of 32 patients, 97% (31 of 32) complained of grip weakness or impaired fine motor skills and 100% had obvious hand muscle atrophy that was most pronounced in the thenar muscles. On examination, the muscle weakness and wasting is in a lower trunk distribution as follows: most pronounced in median nerve-innervated thenar muscles (T1 innervation > C8 innervation), intermediately pronounced in ulnar nerve-innervated hand and forearm muscles (T1 innervation equals C8 innervation), and least pronounced in radial nerve-innervated forearm muscles (C8 innervation without T1 innervation).

Sensory features, although relatively minor in comparison to the motor features, are almost always present. Most patients, in retrospect, acknowledge a long history of intermittent aching and paresthesias in a lower plexus (particularly T1) distribution. In our series of 32 patients, 31 (97%) complained of pain, paresthesias, or numbness in a lower plexus distribution. Of these patients, the sensory abnormalities were restricted to the T1 dermatome in 41% and to the C8 dermatome in 31%. When the C8 axons are severely affected, the T1 > C8 pattern of involvement may not be appreciable.

**EDX Features.** The EDX features associated with TN-TOS correlate well with the pathologic and clinical manifestations, demonstrating a T1 > C8 pattern on both NCSs and needle EMG.
When present, this pattern is essentially pathognomonic.\textsuperscript{1,16,25} Because TN-TOS patients are typically not referred with this diagnosis in mind, they are usually diagnosed by the constellation of EMG findings. Thus, our approach to the EDX assessment of the upper extremity is discussed.

Because the sensory NCS are more sensitive to focal axon loss (the majority of PNS lesions), we begin with them and attempt to localize the lesion. We then perform the motor NCS and define the pathophysiology and severity of the lesion. The needle EMG study is performed last to confirm and fine tune the localization, to further assess lesion severity, and to assess the temporal features of the lesion, including its duration (acute, subacute, or chronic) and rate of progression (slow, intermediate, or rapid). This approach was recently reviewed in great detail\textsuperscript{14} and will only be superficially discussed here. With upper extremity referrals, we start with the median nerve, recording from the index finger (Med-D2), the superficial radial nerve, recording from the dorsum of hand (SR-DH), and the ulnar nerve, recording from the little finger (Uln-D5).

When either the Med-D2 or SR-DH sensory response is abnormal (both assess sensory axons derived from the C6 or C7 dorsal root ganglion [DRG]),\textsuperscript{14,16} we add the lateral antebrachial cutaneous sensory NCS, recording from the lateral forearm (LABC), and the median nerve sensory NCS, recording from the thumb (Med-D1) to better localize the lesion. Both of these studies assess sensory axons derived from the C6 DRG. The pattern of abnormalities typically localizes the lesion.

When the Uln-D5 response is abnormal (assesses sensory axons derived from the C8 DRG), we add the medial antebrachial cutaneous (MABC) sensory NCS, recording from the
The pattern of abnormalities typically localizes the lesion.

With TN-TOS, the screening sensory NCSs typically show a low amplitude Uln-D5 response, which localizes the lesion to the ulnar nerve, medial cord, or lower plexus and prompts the addition of the MABC NCS. Because the latter also is abnormal, the lesion can now be localized to the medial cord or lower plexus. Because the fibrous band stretches the T1 APR > C8 APR, the T1 fibers are affected out of proportion to the C8 fibers. As a result of this inequality, the MABC response (solely or predominantly T1) is affected to a greater degree than is the Uln-D5 response (solely or predominantly C8). In most TN-TOS cases, the MABC response is unelicitable and the ulnar sensory response is abnormally low in amplitude, either below the lower limit of normal (absolute abnormal) or less than 50% of the value recorded from the contralateral side (relative abnormal). In our series of 32 patients, the MABC response was absent in 68%, whereas the Uln-D5 response was absent in only 6% (2 patients). In the other 30 patients, the Uln-D5 response was normal in 3 (9%), relatively abnormal in 25 (78%), and absolutely abnormal in 2 (6%). Thus, the majority demonstrated a relative ulnar response abnormality. This would have been unrecognized had the contralateral Uln-D5 sensory NCS not been performed. Although many anatomic studies have reported that the MABC nerve contains sensory axons derived from both the C8 and T1 DRG more commonly than from the T1 DRG alone, this indicates that the C8 contribution, when present, is insufficient to produce an MABC sensory response abnormality.

On motor NCS testing, consistent with the clinical features, the median motor response, recording from the thenar eminence, is low in amplitude and is affected out of proportion to
either of the 2 ulnar motor responses (recording from the abductor digiti minimi or first dorsal interosseous). Again, this occurs because the thenar muscles receive more T1 than C8 innervation, whereas the ulnar motor responses receive more equal input from C8 and T1. In our series of 32 TN-TOS patients, the median motor response was absent in 1 (3%), low amplitude in 29 (91%), and relatively low in 2 (6%), whereas the ulnar motor response, recording from the hypothenar eminence, was never absent, low amplitude in 1 (3%), relatively low in 12 (38%), and normal in 18 (59%) of patients. The ulnar motor study, recording first dorsal interosseous, showed similar findings. Because the radial motor response, recording from the extensor aspect of the forearm, distally, receives C8 input but typically no T1 input, its involvement is even lower than that of the ulnar motor NCS.

In our series of 32 TN-TOS patients, the incidence of median motor response abnormalities exceeded that of ulnar sensory response abnormalities, consistent with an APR-level lesion. This pattern would be atypical of a medial cord or lower trunk lesion because with focal axon loss processes involving mixed PNS elements (elements containing sensory and motor axons), the sensory response abnormalities are more pronounced than the motor response abnormalities. Consistent with a T1 > C8 pattern, in our study, the most common combination of NCS abnormalities was an abnormal MABC sensory response with an abnormal median motor response (observed in 89%).

On needle EMG, as expected, the abnormalities are in the muscle domain of the lower plexus and, again, are most pronounced in the thenar muscles. The abnormalities indicate a slowly progressive axon loss process: neurogenic recruitment, long duration MUAPs, and a sparse number of low amplitude fibrillation potentials often restricted to the hand muscles,
especially those of the thenar eminence. In our series, chronic changes were noted in all patients, but fibrillation potentials were observed in only about half. When present, they involved the thenar muscles in all cases and the ulnar muscles in two-thirds.

Even with much less severe lesions, the T1 > C8 pattern often is present. For example, one of our patients had the classic MABC > Uln-D5 sensory NCS pattern of TN-TOS on sensory NCS. The motor NCS and needle EMG showed the same pattern. Clinically, he had mild thenar eminence wasting and, in retrospect, a long history of intermittent extremity aching and little finger paresthesias for which he had not sought medical advice. He underwent surgical sectioning of the fibrous band with improvement of his sensory features and cessation of motor feature progression.

It is important to realize that the pathology of TN-TOS is focal axon loss and, therefore, EDX studies that assess propagation speed, such as F-wave latencies and somatosensory evoked potentials, are insensitive. For these studies to be abnormal, the lesion would have to be severe enough to involve all of the faster conducting motor fibers. Consequently, even when abnormal, the information provided is superfluous and less informative than that of the routine EDX studies. Thus, the most sensitive response measurements are those that reflect axon loss (amplitude and negative area under the curve of the response), not slowing (latencies and conduction velocities). With the *triple stimulation technique*, which is an extension of transcranial magnetic stimulation, stimuli are delivered to the scalp, wrist (ulnar motor fibers), and supraclavicular fossa. This technique quantifies the percentage of spinal motor neurons that can be made to discharge (nearly 100% among normal individuals) and, therefore, may identify...
conduction abnormalities involving the lower plexus. Nonetheless, even when abnormal, the information provided is superfluous and less informative than that of the routine EDX studies.

**Differential Diagnosis.** The differential diagnosis of TN-TOS theoretically includes any disorder involving the C8 or T1 spinal cord segment-derived motor or sensory axons. These can be classified anatomically into disorders of the AHC (segmental motor neuron disease), nerve root (C8 or T1 radiculopathies), lower plexus, medial cord and mononeuropathies involving the median or ulnar nerve. Except for advanced carpal tunnel syndrome (CTS) and T1 radiculopathies, none of these entities demonstrate an isolated T1 pattern or a T1 > C8 pattern of deficits and, of these, only AHC disease shows isolated motor abnormalities. Moreover, because of their distinctive histories, examination findings, and EDX features, these entities should not be confused with TN-TOS. For example, AHC disorders are purely motor, the primary feature with radiculopathies is radiating neck pain, medial cord lesions spare the C8-radial nerve innervated muscles, and mononeuropathies usually have sensory > motor deficits and abnormalities confined to a single nerve territory.

**Advanced CTS.** When TN-TOS has a T1 > C8 deficit pattern, the thenar muscles are affected out of proportion to the more balanced C8-T1 muscles. Hence, the thenar muscle involvement mimics advanced CTS (Figure 4). However, the other clinical features are distinctive (Table 2). Clinical features unique to advanced CTS include: (1) initial episodic hand tingling present upon awakening, (2) hand tingling precipitated by activities requiring limb elevation (driving; shaving) that resolve with limb lowering, (3) spontaneous hand tingling when seated at rest, (4) eventual sensory loss in a distal median nerve distribution (palmar cutaneous nerve sparing), (5) frequent onset in the dominant limb or dominant > nondominant limb
involvement, and (6) weakness and wasting restricted to the thenar eminence and lateral 2 lumbrical muscles. Clinical features unique to TN-TOS include: (1) a long history of aching pain in a lower plexus distribution, (2) patchy sensory loss in a lower plexus distribution (often T1 > C8), and (3) weakness and wasting in a lower plexus distribution with T1 > C8 muscles most involved (thenar muscles), C8 = T1 muscles intermediately involved (ulnar muscles), and C8-radial nerve innervated muscles least involved (extensor indicis, extensor pollicis brevis) (Table 2). The EDX features are also discriminatory. With advanced CTS, EDX testing demonstrates a focal median neuropathy located at or distal to the wrist that involves the sensory and motor fibers and is predominantly axon loss in nature, which is quite different from the EDX features of TN-TOS.

C8, T1 Radiculopathies. The segmental distribution of the sensory and motor abnormalities associated with TN-TOS may cause confusion with radicular disorders. Again, the clinical and EDX features of radiculopathies are distinct from those of TN-TOS (Table 2). With radiculopathies, the primary clinical feature is radiating neck pain, which can be precipitated by particular maneuvers, such as sustained neck extension, with or without cervical rotation to the painful side. The sensory abnormalities tend to be more pronounced distally and more pronounced than the motor abnormalities. On EDX testing, because of the intraspinal localization of radiculopathies, the sensory responses are normal. The ulnar and median motor responses are typically normal but can be mildly reduced in amplitude with more severe root involvement. On needle EMG, although the distribution of abnormalities may be similar, they typically are much less pronounced in severity.
**Evaluation.** The major studies used to diagnose TN-TOS are EDX (reviewed above) and radiologic. Cervical spine radiography reliably identifies C7 bony anomalies (oblique views may be required) and can narrow the differential diagnosis. CT and MRI also identify bony anomalies. When patients with TN-TOS have bilateral cervical ribs, the smaller rib is usually responsible.\(^{43}\) Because of its ability to identify or exclude other disorders in the differential diagnosis, MRI is the radiologic study of choice. Because of its radiolucent nature, the fibrous band cannot be imaged by plain films or CT. Likewise, although routine MRI sequences may identify lower plexus distortions, they do not reliably identify fibrous bands.\(^{26,44-46}\) Newer MRI techniques, however, are beginning to overcome this problem.

Filler et al. first described magnetic resonance neurography (MRN) in 1993.\(^{47}\) This technique uses heavy T2 weighting, fat suppression, and pulsation artifact suppression to image peripheral nerves while simultaneously suppressing the surrounding tissue. Common MRN sequences include standard spin-echo T1-weighted images and fast spin-echo T2-weighted images with fat suppression, as well as short tau inversion recovery sequences (to provide intrinsic fat suppression) and a newer protocol, termed SPAIR (T2 spectral adiabatic inversion recovery), which enhances the signal-to-noise ratio and further suppresses fatty tissue.\(^{48}\) This technique, which generates nerve images referred to as neurograms, can demonstrate nerve fiber deviations, such as those resulting from fibrous bands. In addition, the fibrous band itself can be imaged.\(^{48,49}\) Another MR technique, termed “tractography,” uses diffusion tensor imaging to image peripheral nerve fascicles.\(^{50}\) This technique is based on the principle that water molecules move through nerve fiber bundles in a nonrandom manner. These 2 MR techniques, when they are able to visualize the site and cause of compression, improve diagnostic certainty and allow
the surgeon to individualize the planned decompressive surgery, thereby lessening the associated surgical morbidity.

**Treatment and Prognosis.** Because of its slowly progressive nature, reinnervation via collateral sprouting initially keeps pace with denervation. Thus, conservative treatment has no role in the treatment of TN-TOS, which is always treated surgically with band sectioning. Because the band is supraclavicular in its location, a supraclavicular approach is preferred; a transaxillary approach is too distant and provides inadequate visualization.\(^{24,26,51-53}\) In addition to band sectioning, the distal aspect of the C7 bony anomaly is often removed. The FTR, when normal, should be left in place.\(^5^4\)

Once the fibrous band is sectioned, the affected nerve fibers are no longer stretched. Clinically, the aching and paresthesias or dysesthesias resolve. Although the weakness and atrophy stop progressing, significant motor improvement is unexpected because: (1) the distance between the lower plexus lesion and the denervated hand and distal forearm muscles is too great for proximodistal axon advancement and (2) collateral sprouting is already maximal.

**CONCLUSION**

The term “thoracic outlet syndrome” should not be used in the singular because it reflects a group of distinct disorders with differing etiologies, clinical features, evaluations, and treatments.

The T1 > C8 pattern of nerve fiber involvement associated with most cases of TN-TOS reflects its underlying pathophysiology, its clinical and EDX manifestations, and its appropriate treatment. Because the EDX manifestations are essentially pathognomonic, they must be
recognized by EDX providers. The second part of this review will focus on arterial, venous, traumatic neurovascular, and disputed TOS.
REFERENCES


17. Waller A. Experiments on the section of the glossopharyngeal and hypoglossal nerves of the frog, and observations of the alterations produced thereby in the structure of their primitive fibres. Philosophical Transactions of the Royal Society of London 1850;140:423-429.


Table 1. The muscle domains of the lower plexus elements (with their nerve innervation).

<table>
<thead>
<tr>
<th>The lower plexus*</th>
<th>The C8 anterior primary ramus</th>
<th>The T1 anterior primary ramus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radial nerve</strong></td>
<td>TC‡, anconeus, ED, ECU, APL, EI, EPB, EPL</td>
<td>Ulnar nerve</td>
</tr>
<tr>
<td><strong>Ulnar nerve</strong></td>
<td>FCU, FDP-3/4, ADM, AP, interossei, third and fourth lumbricals, ODM, FPB (deep head)</td>
<td></td>
</tr>
<tr>
<td><strong>Median nerve</strong></td>
<td>FDS, PL, FPL, PQ, APB, OP, FPB (superficial head), first and second lumbricals</td>
<td>Median nerve</td>
</tr>
<tr>
<td>*The muscle domain of the lower plexus is the summation of the muscle domains of its elements (i.e., the C8 APR, the T1 APR, and the lower trunk).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The lower trunk†</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radial nerve</strong></td>
<td>TC, anconeus, ED, ECU, APL, EI, EPB, EPL</td>
</tr>
<tr>
<td><strong>Ulnar nerve</strong></td>
<td>FCU, FDP-3/4, ADM, AP, interossei, third and fourth lumbricals, ODM, FPB (deep head)</td>
</tr>
<tr>
<td><strong>Median nerve</strong></td>
<td>FDS, PL, FPL, PQ, APB, OP, FPB (superficial head), first and second lumbricals</td>
</tr>
<tr>
<td>†The muscle domain of the lower trunk is the summation of the muscle domains of the C8 root and the T1 root.</td>
<td></td>
</tr>
</tbody>
</table>

ADM, abductor digit minimi; AP, adductor pollicis; APB, abductor pollicis brevis; APL, abductor pollicis longus; APR, anterior primary ramus; ECU, extensor carpi ulnaris; ED, extensor digitorum; EI, extensor indicis; EPB, extensor pollicis brevis; EPL, extensor pollicis longus; FCU, flexor carpi ulnaris; FDP, flexor digitorum profundus; FDS, flexor digitorum
superficialis; FPB, flexor pollicis brevis; FPL, flexor pollicis longus; ODM, opponens digiti minimi; OP, opponens pollicis; PL, palmaris longus; PQ, pronator quadratus; TC, triceps
Table 2. Distinguishing clinical features: late CTS, TN-TOS, and radiculopathies (C8, T1).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Advanced CTS</th>
<th>TN-TOS</th>
<th>C8 or T1 radiculopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Upper extremity aching typically occurs with more advanced CTS</td>
<td>Long history of aching along the lower plexus distribution</td>
<td>Neck pain radiating into upper extremity; precipitated by neck positioning</td>
</tr>
<tr>
<td>Tingling</td>
<td>Remote history of episodic hand tingling at rest and with elevation</td>
<td>Infrequent</td>
<td>Often concomitant with the radiating pain</td>
</tr>
<tr>
<td>Sensory loss</td>
<td>Median nerve distribution, especially distal aspects of the index and middle fingers</td>
<td>Lower plexus distribution; less pronounced than weakness</td>
<td>Dermatomal, but often restricted to distal portion of dermatome; often more pronounced than the weakness</td>
</tr>
<tr>
<td>Weakness</td>
<td>Median nerve-innervated distal to wrist</td>
<td>Lower plexus distribution; T1 &gt; C8</td>
<td>Myotomal distribution</td>
</tr>
<tr>
<td>Atrophy</td>
<td>Thenar eminence (moderate-to-severe)</td>
<td>Thenar eminence (more severe) and medial and distal forearm (less apparent)</td>
<td>Myotomal distribution</td>
</tr>
</tbody>
</table>

CTS, carpal tunnel syndrome; TN-TOS, true neurogenic thoracic outlet syndrome
Figure Legends

Figure 1. The neural and vascular elements of the thoracic outlet. (From Ferrante MA. The thoracic outlet syndromes. Muscle Nerve 2012;45:780-795. Fig 1, p 781. This material is reproduced with permission from John Wiley and Sons, Inc.)

Figure 2. The interscalene triangle and surrounding structures. In this sagittal MR image, the superior borders of the interscalene triangle (the anterior scalene muscle [ASM] and the middle scalene muscle [MSM]) are shown. The relationship between the ASM and the subclavian vein (SV) and subclavian artery (SA) are also apparent. The C7, C8, and T1 nerve roots and the clavicle (C) are also identified. (From van Es HW, Bollen TL, van Heesewijk HPM. MRI of the brachial plexus: a pictorial review. Eur J Radiol 2010:74;391-402. This material is reproduced with permission from Elsevier.)

Figure 3. Normal anatomical relationship between the first thoracic rib (R1) and the C8 and T1 roots. From this image, it can be appreciated that the T1 root lies below R1, whereas the C8 root lies above it. Consequently, when these 2 roots are displaced upward, the T1 root is more affected than the C8 root. The C5, C6, and C7 nerve roots are also identified. (From van Es HW, Bollen TL, van Heesewijk HPM. MRI of the brachial plexus: a pictorial review. Eur J Radiol 2010:74;391-402. This material is reproduced with permission from Elsevier.)

Figure 4. Right thenar eminence wasting in a patient with advanced carpal tunnel syndrome (A) and another with true neurogenic thoracic outlet syndrome (B).