The Tethered Cord Syndrome and Its Occult Form

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Congenital Spinal Defects Cause Stretching/Tethering of the Spinal Cord

A clinical description of the spinal cord under undue tension first appeared in the medical literature in 1857. Johnson reported a pediatric patient with a "fatty tumor of the sacrum…connected with the spinal membranes" [1]. Eighteen years later, Jones (1891) described the first surgical intervention on the spine to relieve pressure on the cauda equina [2]. Another few passed before Fuchs (1910) hypothesized that the intermittent incontinence seen in patients with myelomeningocele was due to increased tension on the distal spinal cord during flexion [3]. Lichtenstein was the first to employ the term "spinal dysraphism," and although he helped further the concept of cord dysfunction secondary to tethering lesions, his hypothesis linking this to the Chiari malformation was ultimately not accepted [4, 5]. Subsequent articles continued to expand on distal spinal cord disorders such as sacral lipomas and occult spinal dysraphism (OSD), although they made little reference to any tethering effect, and instead attributed neurological deficits to lipomatous infiltration or congenital neuronal dysgenesis [6, 7].

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The Tethered Cord Syndrome Is the Clinical Manifestation of Such Stretching

Surprisingly, the filum terminale was not mentioned in the context of a tethered spinal cord until Garceau's description in 1953 of "filum terminale syndrome" involving three patients demonstrating clinical improvement following lumbar laminectomy and the severing of a thick, tight filum terminale [8]. Garceau's findings implicating a tight filum terminale in spinal cord tension-induced neurological dysfunction were later supported by the work by Jones and Love and by James and Lassman [9, 10].

Evidence of Tethered Cord Syndrome (TCS)

Anatomical

Anatomical correlations of the clinical manifestations of a tethered conus were first introduced by Fitz and Hardwood in 1975 with their classification of a "conus tip below the L2-3 interspace in a child older than five years" and a "filum measuring greater than two mm on myelography" as abnormal [11] (Fig. 8.1). Subsequently, there was no concrete definition of the syndrome until the 1976 surgical series by Hoffman et al., describing 31 patients with symptomatic improvement following

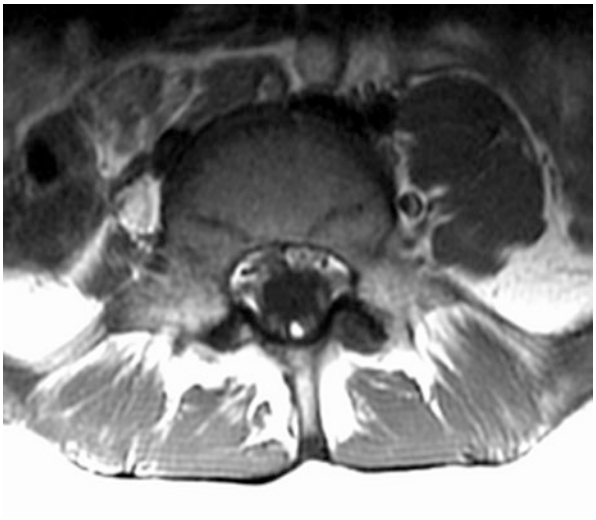

Fig. 8.1 An 11-year-old female who remained unable to walk until 4 years of age. She presented with chronic progressive back pain, progressive lower extremity weakness, and progressive bladder incontinence. The figure shows a T1-weighted axial image of the mid-lumbar spine depicting a thick and fatty filum terminale. The conus medullaris is low lying, terminating at the mid-L3 vertebral level. This case represents a typical symptomatic TCS patient

sectioning of a thickened, tight filum. This was the first clinical description of "tethered cord syndrome" (TCS) and helped establish a "low conus medullaris and a thickened filum terminale measuring 2 mm or more in diameter" as diagnostic criteria [12–16].

Physiological/Experimental

Despite an impressive body of clinical evidence describing the associated motor and sensory changes, there remained a relative lack of mechanistic understanding of the presumed neuronal dysfunction in TCS. In 1981, Yamada et al. provided the most compelling evidence for a possible mechanism [17]. Defining TCS as a "stretch-induced functional disorder of the lumbosacral spinal cord," they used human and feline experimental models to establish that caudal traction on the distal spinal cord results in diminished blood flow and a semi-reversible impairment in oxidative metabolism that manifests as neurological deficits. Both the degree and reversibility of cord dysfunction depend on the magnitude and duration of cord traction. The authors also concluded that chronic tension leads to pre-loading of the distal spinal cord, allowing severe and permanent injury to occur as a result of even minor additional stretching [18–20]. Kocak et al. reported similar findings using a guinea pig model [21].

The Basic TCS Anomaly Is the Tight Filum Terminale

Low-Lying Conus Medullaris

Yamada [19] summarized his findings in a description of TCS that included updated diagnostic imaging criteria in the form of (1) a thick filum terminale (>2 mm in diameter) and/or a structural decrease in viscoelasticity (fibroadipose tissue, etc.), (2) an elongated spinal cord, and, uniquely, (3) posterior displacement of the conus medullaris with the filum terminale pressed against the thecal sac. Although the level of the conus tip was deemed nonessential in this summary, this diagnostic criterion has obviously persisted [13, 19, 22].

Classic TCS Surgical Series

This new pathophysiological evidence behind TCS coincided with an effort at better establishing the surgical experience associated with cord untethering. In one of the first relevant surgical series on TCS, Pang et al. reported on 23 adult patients [22]. All 23 met TCS criteria on the basis of a conus tip "below the lower border of the L2 vertebral body" and a spectrum of preoperative signs and symptoms that included pain, sensorimotor deficits, urinary bladder dysfunction, bowel dysfunction, and cutaneous manifestations. The authors reported postoperative improvement in pain

and sensorimotor deficits in 83.3% and 86.7% of patients, respectively, with modest improvement recorded for bladder dysfunction (38.5%) but no improvement in bowel dysfunction. This pattern has been replicated, with more recent reports demonstrating the successful stabilization of neurological decline and a consistently high rate of postoperative pain resolution, both within the 80–100% range. Rates of improvement following untethering have been more variable regarding other common preoperative complaints such as urological dysfunction [19, 23–26]. While other literature has confirmed Pang's findings of rates of improvement as high as 87%, several other reports and reviews show rates of improvement as low as 16% [22, 25, 27–31]. Admittedly, much of this variability is due to differences in the way outcomes are measured.

TCS from Other Lumbar Spinal Anomalies

In addition to breaking ground on the pathophysiology behind TCS, Yamada et al. also broadened the clinical definition of TCS by correlating the stretch-induced cord dysfunction seen in this condition with similar neurological changes in patients with other distal cord anomalies such as myelomeningocele, lipomyelomeningocele, and other forms of spinal dysraphism [17]. These observations were published within a year of the similar conclusions by James and Lassman in their classic monograph "Spina Bifida Occulta," which implicated spinal cord tethering in a variety of dysraphic lesions including lipomyelomeningocele, diastematomyelia, meningocele manqué, and dermal sinus tract. Nevertheless, as more and more cases appeared in the literature, the trend was clearly toward a more inclusive etiological differential for TCS secondary to some form of cord tethering.

Emergence of OTCS

TCS in Patients with Normal Conus and Filum Anatomy (Occult TCS)

Hoffman et al. deepened this diagnostic spectrum with a second surgical series demonstrating clinical improvement in patients who presented with the characteristic neurological findings of TCS together with myelographic abnormalities. However, this subsequent surgical description included a subset of patients whose sole anatomical finding was a "tight filum," defined only by its tendency to "spring apart when transected" intraoperatively. Despite a normally positioned conus and non-thick filum terminale, TCS was diagnosed in these patients, and surgery was performed given only a combination of "classical" signs and symptoms and the presence of bony spina bifida occulta [32–34]. This series set the stage for the diagnosis of TCS in the absence of a low-lying conus and eventually an array of controversial papers on "occult tethered cord syndrome" (OTCS).

TCS with Conus in Normal Position (Warder and Oakes)

During the past two decades, a number of authors have offered evidence to support operating on patients with TCS-like symptoms with a normally positioned conus. In their retrospective series involving 13 patients with TCS "in whom the spinal cord terminated at or above the L1–L2 disc space," Warder and Oakes were the first to discuss the criteria for operating on TCS patients without a low-lying conus medullaris (Fig. 8.2). Given a history significant for incontinence and spina bifida occulta, the authors selected patients on the basis of cutaneous, neurological, and/or anatomical findings, most frequently including filar lipomas. Ten (77%) of these patients presented with neurological deficits. Lower extremity weakness, spasticity/hyperreflexia, and bladder dysfunction were the most common complaints, each occurring in four of ten (40%) patients. Bowel dysfunction was slightly less common, occurring in three of ten (30%). Cutaneous stigmata including lumbosacral

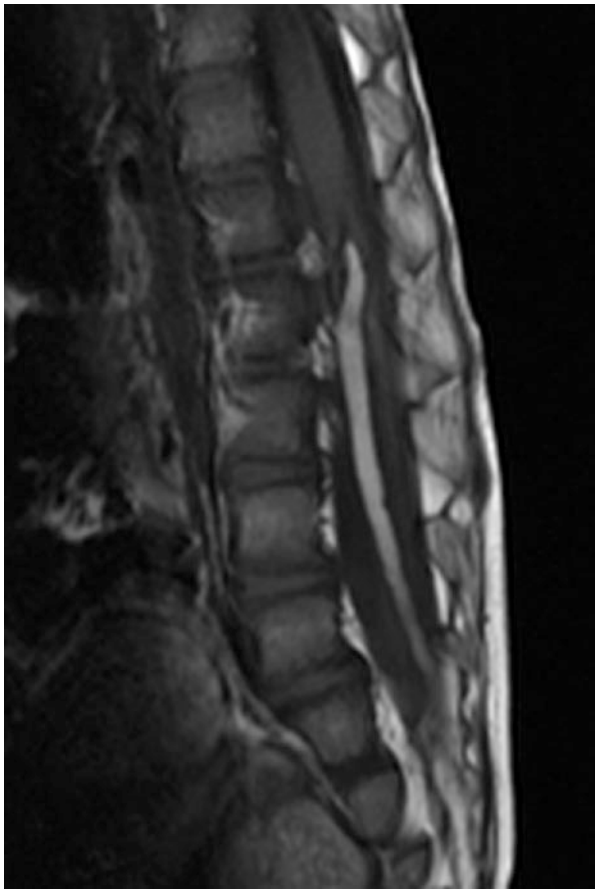

Fig. 8.2 TCS with conus in normal position. An 18-month-old female with multiple congenital abnormalities who presented with progressive scoliosis. The figure shows a T1-weighted midsagittal MR image of a very thick and fatty filum terminale with a normally positioned conus medullaris at the L1 vertebral level. The abnormal filum in this case cannot be denied, and most surgeons would choose to treat. However, the natural history and cause and effect between TCS and scoliosis can be questioned

hemangioma, lumbosacral subcutaneous lipoma, and a midline skin tag were identified in 4 of 13 (31%), 1 of 13 (8.5%), and 1 of 13 (8%) patients, respectively. Extremity abnormalities including leg length discrepancy and foot deformities were present in 3 of 13 (23%) and 2 of 13 (15%), respectively. Radiographic findings consisting primarily of bifid vertebrae were reported in 10 of 13 (77%) patients. Intradural pathologies of occult spinal dysraphism including lipoma of the filum, diastematomyelia, meningocele manqué, and syringomyelia were present in eight of ten (80%) patients. Fat in the filum terminale was confirmed "either microscopically or radiographically" in 12 of 13 patients (92%). Outcomes were based on a reassessment of presenting symptoms and their categorization as improved, unchanged, or worsened during a follow-up period of 6 months to 6 years. The authors reported "improvement or stabilization of the majority of the presenting neurological complaints" and endorsed the consideration of filum release in this population of patients [35–37]. Although they were appropriately cautious about their assertions, this article still succeeded in setting a precedent for the surgical management of TCS in patients with a normally positioned conus.

Did These Patients Have OTCS?

At the most superficial level, one must first consider the exact diagnosis in this cohort of patients. Warder et al. defined their surgical indications clearly and attempted to establish a diagnosis of TCS in all of their patients. Not surprisingly, they made sure to emphasize the presence of either cutaneous or anatomical hallmarks of occult spinal dysraphism. In the absence of a more concrete definition of OTCS and lacking any evidence to suggest otherwise, these patients all fell within the growing gray area between OTCS and classic TCS. Cautionary claims aside, a cursory analysis of this series yields room for interpretation. Foremost among the causes of irresolution is the bias inherent in relying on patient reports for outcomes data, and data indicating 20–50% prevalence of bony spina bifida occulta and a 6% incidence of fat in the filum terminale in the general population [35, 38] (Fig. 8.3). Consequently, this paper did little to dispel the mystery surrounding OTCS.

Diagnosed OTCS Surgical Series (Nazar et al.)

In stark contrast, Nazar et al. reported 32 definitive cases of "occult tethered cord syndrome" (OTCS) in their pediatric surgical series [39]. Presenting problems included severe back and/or leg pain, daytime urological problems, encopresis, or a combination of symptoms. In addition to a thorough history and physical examination, each patient was imaged via lumbar and sacral spine X-rays, lumbar MRI, and CT/myelography. Patients presenting with urological symptoms underwent pre- and postoperative urodynamic studies to assess detrusor hyperreflexia. Outcomes included a comparison of pre- and postoperative pain symptomology, the ability to return to performing a full range of physical activities, urodynamic studies when applicable,

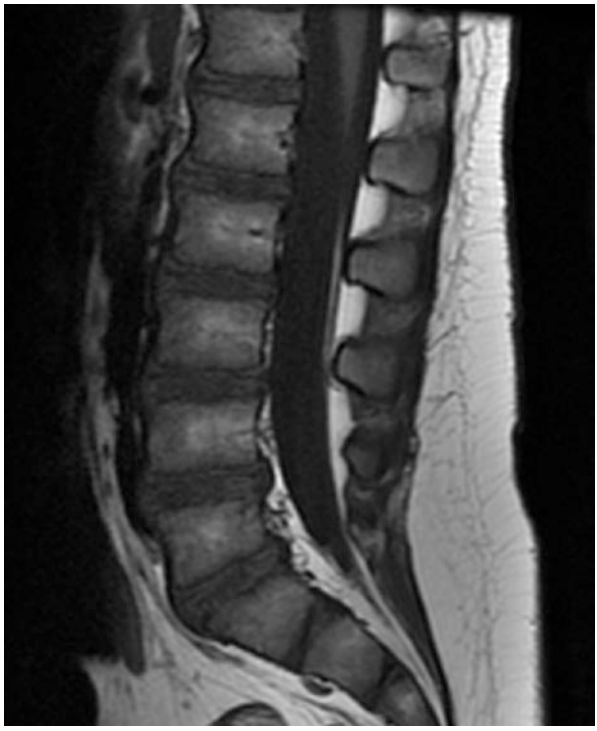

Fig. 8.3 A 6-year-old male with a symptomatic Chiari I malformation in the absence of symptoms of a tethered cord. The figure shows a T1-weighted midsagittal MR image of a thick and fatty filum terminale with a normally positioned conus medullaris at the L1 vertebral level. Should this filum be considered abnormal?

and the percentage decrease in reported urinary incontinence/frequency/urgency. Pain was the most common complaint and was present in 22 of 32 (69%) patients. Pain was the only complaint in 9 of the 32 (28%) and was associated with other symptoms in 13 (41%). Daytime urological dysfunction was present in 22 of 32 (69%) patients and was associated with pain in 10 of 32 (31%). Preoperative urodynamic studies were obtained in 20 patients and revealed small bladders, early detrusor contractions, and poor sensation in most cases. Bowel incontinence was present in 11 of 32 (34%) patients preoperatively. Physical findings other than those associated with pain were largely absent, and only 2 of 32 (6%) patients displayed cutaneous markings typically associated with spina bifida occulta in the form of a cutaneous lumbar hemangioma and lumbar hypertrichosis. Only 3 of 32 (9%) patients presented with an abnormal neurological exam in the form of absent ankle jerk in two and lower extremity weakness with an associated limp in one. MR imaging confirmed the tip of the conus medullaris above the L2 vertebral body and a lipoma-free filum terminale measuring less than 2 mm throughout its entire course in all 32 patients. Lumbar X-rays identified bony spina bifida occulta in 28 of the 32 (88%). The filum terminale was identified and sectioned intraoperatively in all 32 patients, and histological examination confirmed a normal-appearing filum without fat infiltration, scarring, or hemorrhage. During follow-up of 2–48 months, pain was relieved in 22 patients, all of whom returned to full independent activity. Daytime urinary bladder function normalized in

14 of the 22 patients (64%) and showed 50% or greater improvement with respect to a decrease in frequency/urgency/incontinence in 7 of the 22 (32%) postoperatively. Similarly, eight of nine (89%) patients demonstrated increased bladder capacity and sensation during postoperative urodynamic testing. Interestingly, only nine patients underwent urodynamic assessment postoperatively compared to 20 prior to surgery. Stool incontinence resolved in 9 of 11 patients (82%). Despite their willingness to commit to a diagnosis of OTCS, Nazar et al. largely avoided drawing conclusions from their observations in a pattern similar to Warder and Oakes, simply stating that "sectioning of a normal-appearing filum terminale appeared beneficial in the majority of patients." Although cautiously nonconclusive in practice, it became harder and harder to ignore the impact of multiple surgical series describing positive operative outcomes in patients with either OCTS or, more confusingly, a TCS-like syndrome with imaging abnormalities that, if not absent, at least did not fit the previously established "classic" criteria of TCS (Fig. 8.4).

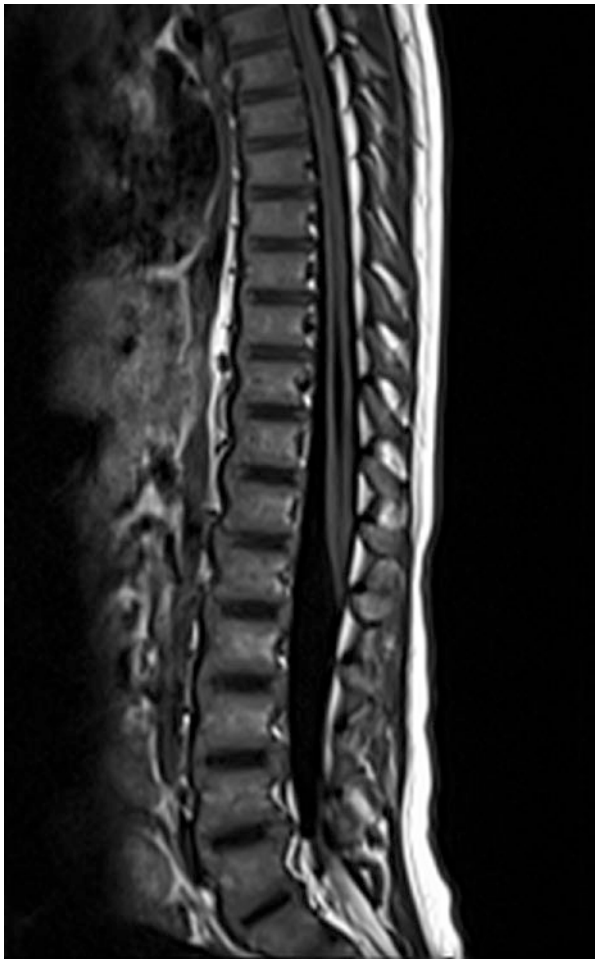

Fig. 8.4 A 4-year-old male with history of a progressive neurogenic bladder (worsening urodynamics) and lower extremity fatigue, a normal neurological examination, and a thin distal spinal cord syrinx. This is a T1-weighted midsagittal MR image showing the syrinx, as well as a posteriorly displaced conus medullaris ending at the L1 spinal level. There is no evidence of a Chiari I malformation, spinal cord tumor, or other possible etiologies of the syrinx. This case illustrates the gray zone between TCS and OTCS. The only abnormalities on this scan are the syrinx and, according to some authors, a posteriorly displaced conus

Is OTCS a Real Diagnosis?

Signs and Symptoms Occur in Normal Patients

The first issue to examine is the actual existence of OCTS. As we have discussed in some detail, much of the confusion surrounding the diagnosis lies in differing definitions. The combination of a broad spectrum of etiologies, all possibly leading to the same stretch-induced pathophysiology behind TCS, and the increasingly popular practice of surgical management in the absence of radiographic findings has left substantial room for interpretation. This is concerning, since in the context of normal imaging, many of the symptoms used to diagnose OTCS including back pain and urological dysfunction have a relatively high prevalence in otherwise healthy populations. For example, low back pain has a prevalence ranging from 24% to 58% in school-aged children between the ages of 11 and 14 years [40–42]. Similarly, urinary bladder incontinence is a problem affecting 20–40% of office visits to pediatric urologists with a prevalence rate between 11% and 20% among children in the 4–10 year age range [43–45]. Given the marked improvement in urinary incontinence reported after cord untethering, it is important to note that in most cases of pediatric urinary incontinence, the differential diagnosis list can be extensive, and there is spontaneous improvement in almost 90% [45, 46]. This raises several questions regarding both the diagnosis of OTCS and any benefit derived from filum sectioning versus time and medical management [47].

Do We Need to Operate on OTCS Patients?

Beyond the immediate symptomatic improvement described following filum sectioning, the decision to operate in the context of cord tethering is frequently predicated on a natural history for tethering lesions, occult or otherwise, that is described as both progressive and inevitable [17, 34, 48, 49]. Some recent evidence suggests that clinical deterioration is not inevitable in this patient population. In their small retrospective analysis, Steinbok et al. described 15 cases of children with refractory urinary incontinence and "possible OCTS" based on a normally positioned conus and no other visible explanation for urinary incontinence. Following discussions with families about filum sectioning as an "unproven but potentially beneficial procedure," eight chose surgery, and seven chose more conservative measures. After a mean follow-up of 3.3 years, there was no evidence of deterioration in any of the conservatively managed patients, and 29% of them showed some improvement in their symptoms [50]. This must of course be compared with the 88% of patients who showed symptomatic improvement following surgery. However, it is most concerning that much of the literature surrounding filum sectioning in OTCS lacks a benchmark for significance, yet there is a widespread disagreement about both the diagnosis and the treatment of OTCS, most physicians expressing unease about the practice [51]. Such a wide distribution in the absence of concrete data is surprising and questions our contemporary threshold for what we claim to be data-driven changes in clinical practice.

No Established Diagnostic Tests

Although a patient population exhibiting the clinical picture of TCS in the absence of lumbar cord abnormalities is possible, if not likely, the relative size of that population is unknown. Accordingly, what needs to be rigorously established is a minimum constellation of signs and symptoms warranting surgical intervention. Along these lines, some have proposed additional noninvasive testing to identify patients with suspected OTCS given the diagnostic limits of urodynamic testing. One example involves the use of dynamic structural imaging of the spine via ultrasonography and more recently cine MR to assess for tethering and decreased motion [52, 53]. Yamada et al. have proposed the assessment of anal sphincter tone and posterior displacement of a normally positioned conus as criteria for diagnosis [54]. However, there is an almost complete lack of normal or pathological reference data with which to determine the sensitivity and/or specificity of these tests. Until such validation emerges, surgical management of OTCS will continue to be based largely on provider preference and clinical judgment. Nevertheless, the surgical management of OTCS is now established practice in some centers, and the main challenge for the future will be to establish more concrete diagnostic criteria. These criteria will require large cohorts comprising separate surgically and conservatively managed study arms if they are to achieve the necessary impact. However, given the previously established benefit of untethering in the context of symptomatic cord stretching, the question becomes one of ethics. Appreciating the current landscape of surgery for OTCS, some centers manage virtually every patient surgically, while others manage none in this manner. One option would be to match OTCS surgical centers to nonsurgical centers through registries and to measure standardized outcomes between their respective patient populations. However, as we slowly approach the realization of large-scale surgical series for OTCS and the need to juxtapose "OTCS" presentations against the accepted "standard" TCS presentations, it would be sensible to begin by examining what most of the pediatric neurosurgery community considers to represent standard of care in the diagnosis of TCS, the evolution of its management, and how these standards were reached. It would be unwise either to adopt or to reject indications for a procedure (e.g., OTCS) without reasonable knowledge of the burden of evidence used to establish similar indications for a comparable standard of care (TCS).

The Standard of Care of TCS

First described nearly two centuries ago, TCS has had a uniquely controversial history. Pioneered during an era of widespread surgical discovery, it is possible that cord untethering to treat TCS has been grandfathered into current clinical practice and has yet to be viewed through the modern lens of evidence-based medicine. With a more procedurally permissive blurring of lines driven by OTCS, some might wonder at the percentage of TCS diagnoses that have resulted in unwarranted surgical intervention over the years. This concept of overtreatment is of growing concern in healthcare

with examples in many disciplines. For example, the overdiagnosis of invasive breast cancer among women in their 50s is estimated to be as high as 54% [55, 56]. Similarly, in the context of a steadily rising incidence of thyroid cancer since 1973, many new diagnoses have been of smaller and less aggressive cancers requiring no treatment [57]. Nearly every example is a result of improvements in screening and diagnostic technology, which inevitably result in increased detection of subclinical disease. This, in turn, leads to an overestimation of the benefits of certain therapies based on the treatment of milder disease forms. The evolution of TCS, in contrast, has not followed this pattern; diagnosis has been largely led by natural history data demonstrating deterioration over time in the absence of surgical intervention, which easily outweighs the fairly low risk of surgical complications in the context of relatively simple defects (e.g., tight filum terminale, dermal sinus tract) [58–64]. It is not the purpose of this chapter to review the surgical indications of TCS, as these studies are reviewed elsewhere in this book. However, a sense of generalization of both the therapeutic benefits of surgery and the detrimental effects of conservatism seems to have permeated the literature inextricably during the last three decades. On the one hand, this eventually led to the scientifically unproven concept of OTCS being encompassed within the surgical armamentarium; at the other extreme, it led equally conscientious surgeons to question the status quo and state that surgery is seldom, if ever, necessary in any of these disorders [65–67]. It may be time for large cohort studies and registries to help us determine not only what works or does not work but, more importantly, what is appropriate in the context of specific diagnoses (tight filum terminale, split cord malformation, lipomyelomeningoceles, and even lipomyelomeningocele subtypes, etc.), age, imaging findings, and symptomatic states. As has been demonstrated in other medical disciplines, the answer is likely to prove more complicated than assumed by either school [68–70].

Does This Represent a Larger Problem?

First announced in the early 1990s, evidence-based medicine is a relatively new paradigm aimed at improving healthcare. Evidence-based medicine is defined as "the conscientious and judicious use of current best evidence in conjunction with clinical expertise and patient values to guide health care decisions" [71, 72]. What constitutes "best evidence" is assessed on the basis of different levels of evidence, with systematic reviews topping the list. As is the case with TCS, "when definitive evidence is not available, one must fall back on weaker evidence" and ultimately accept "that physicians who are up-to-date as a function of their ability to read the current literature critically… are able to distinguish strong from weaker evidence… are likely to be more judicious… [and] make more accurate diagnoses" [72, 73]. Can we truly claim that this is the case for OTCS? The cliché "hindsight is 20/20" can be applied broadly in the history of medicine and especially surgery. Although we cannot look into the future to identify our current follies, we do possess foresight, the full potential of which we cannot achieve without an honest look at our practices and a reassessment of what we do and why.

References

1. Johnston A. Fatty tumor from the sacrum of a child connected with the spinal membranes. Trans Pathol Soc Lond. 1857;8:16–8.
2. Jones W. Spina bifida occulta: no paralytic symptoms until seventeen years of age: spine trephined to relive pressure on the cauda equina: recovery. Brit Med J. 1891;1:173–4.
3. Fuchs A. Ueber Beziehungen der Enuresis nocturna zu Rudimentärformen der Spina bifida occulta (Myelodysplasie). Wien Med Wochenschr. 1910;80:1569–73.
4. Lichtenstein BW. Spinal dysraphism: spina bifida and myelodysplasia. Arch Neurol Psychiatry. 1940;44(4):792–809.
5. Barry A, Patten BM, Stewart BH. Possible factors in the development of the Arnold-Chiari malformation. J Neurosurg. 1957;14(3):285–301.
6. Bassett RC. The neurologic deficit associated with lipomas of the cauda equina. Ann Surg. 1950;131(1):109–16.
7. Rogers HM, Long DM, Chou SN, French LA. Lipomas of the spinal cord and cauda equina. J Neurosurg. 1971;34(3):349–54.
8. Garceau GJ. The filum terminale syndrome (the cord-traction syndrome). J Bone Joint Surg Am. 1953;35-A(3):711–6.
9. Jones PH, Love JG. Tight filum terminale. AMA Arch Surg. 1956;73(4):556–66.
10. James CCM, Lassman LP. Spina bifida occulta. In: Orthopedic, radiological and neurosurgical aspects. London: Academic Press Inc; 1981.
11. Fitz CR, Harwood Nash DC. The tethered conus. Am J Roentgenol Rad Ther Nuc Med. 1975;125(3):515–23.
12. Barson AJ. The vertebral level of termination of the spinal cord during normal and abnormal development. J Anat. 1970;106(Pt 3):489–97.
13. Hoffman HJ, Hendrick EB, Humphreys RP. The tethered spinal cord: its protean manifestations, diagnosis and surgical correction. Childs Brain. 1976;2(3):145–55.
14. Raghavan N, Barkovich AJ, Edwards M, Norman D. MR imaging in the tethered spinal cord syndrome. AJR Am J Roentgenol. 1989;152(4):843–52.
15. Naidich TP, Harwood-Nash DC, McLone DG. Radiology of spinal dysraphism. Clin Neurosurg. 1983;30:341–65.
16. Hall WA, Albright AL, Brunberg JA. Diagnosis of tethered cords by magnetic resonance imaging. Surg Neurol. 1988;30(1):60–4.
17. Yamada S, Zinke DE, Sanders D. Pathophysiology of "tethered cord syndrome". J Neurosurg. 1981;54(4):494–503.
18. Tani S, Yamada S, Knighton RS. Extensibility of the lumbar and sacral cord. Pathophysiology of the tethered spinal cord in cats. J Neurosurg. 1987;66(1):116–23.
19. Yamada S, Lonser RR. Adult tethered cord syndrome. J Spinal Disord. 2000;13(4):319–23.
20. Lew SM, Kothbauer KF. Tethered cord syndrome: an updated review. Pediatr Neurosurg. 2007;43(3):236–48.
21. Kocak A, Kilic A, Nurlu G, et al. A new model for tethered cord syndrome: a biochemical, electrophysiological, and electron microscopic study. Pediatr Neurosurg. 1997;26(3):120–6.
22. Pang D, Wilberger JE Jr. Tethered cord syndrome in adults. J Neurosurg. 1982;57(1):32–47.
23. Huttmann S, Krauss J, Collmann H, Sorensen N, Roosen K. Surgical management of tethered spinal cord in adults: report of 54 cases. J Neurosurg. 2001;95(2 Suppl):173–8.
24. Iskandar BJ, Fulmer BB, Hadley MN, Oakes WJ. Congenital tethered spinal cord syndrome in adults. J Neurosurg. 1998;88(6):958–61.
25. Lee GY, Paradiso G, Tator CH, Gentili F, Massicotte EM, Fehlings MG. Surgical management of tethered cord syndrome in adults: indications, techniques, and long-term outcomes in 60 patients. J Neurosurg Spine. 2006;4(2):123–31.
26. Gupta SK, Khosla VK, Sharma BS, Mathuriya SN, Pathak A, Tewari MK. Tethered cord syndrome in adults. Surg Neurol. 1999;52(4):362–9; discussion 370

27. Guerra LA, Pike J, Milks J, Barrowman N, Leonard M. Outcome in patients who underwent tethered cord release for occult spinal dysraphism. J Urol. 2006;176(4 Pt 2):1729–32.
28. Selden NR. Occult tethered cord syndrome: the case for surgery. J Neurosurg. 2006;104(5 Suppl):302–4.
29. Fone PD, Vapnek JM, Litwiller SE, et al. Urodynamic findings in the tethered spinal cord syndrome: does surgical release improve bladder function? J Urol. 1997;157(2):604–9.
30. Giddens JL, Radomski SB, Hirshberg ED, Hassouna M, Fehlings M. Urodynamic findings in adults with the tethered cord syndrome. J Urol. 1999;161(4):1249–54.
31. Kondo A, Gotoh M, Kato K, Saito M, Sasakibara T, Yamada H. Treatment of persistent enuresis. Results of severing a tight filum terminale. Brit J Urol. 1988;62(1):42–5.
32. Yamada S, Won DJ. What is the true tethered cord syndrome? Childs Nerv Syst. 2007;23(4):371–5.
33. Yamada S, Won DJ, Pezeshkpour G, et al. Pathophysiology of tethered cord syndrome and similar complex disorders. Neurosurg Focus. 2007;23(2):E6.
34. Hendrick EB, Hoffman HJ, Humphreys RP. The tethered spinal cord. Clin Neurosurg. 1983;30:457–63.
35. Gregerson DM. Clinical consequences of spina bifida occulta. J Manip Physiol Ther. 1997;20(8):546–50.
36. Warder DE, Oakes WJ. Tethered cord syndrome: the low-lying and normally positioned conus. Neurosurgery. 1994;34(4):597–600; discussion 600
37. Warder DE, Oakes WJ. Tethered cord syndrome and the conus in a normal position. Neurosurgery. 1993;33(3):374–8.
38. McLendon RE, Oakes WJ, Heinz ER, Yeates AE, Burger PC. Adipose tissue in the filum terminale: a computed tomographic finding that may indicate tethering of the spinal cord. Neurosurgery. 1988;22(5):873–6.
39. Nazar GB, Casale AJ, Roberts JG, Linden RD. Occult filum terminale syndrome. Pediatr Neurosurg. 1995;23(5):228–35.
40. Balague F, Dudler J, Nordin M. Low-back pain in children. Lancet. 2003;361(9367):1403–4.
41. Altaf F, Heran MK, Wilson LF. Back pain in children and adolescents. Bone Joint J. 2014;96-B(6):717–23.
42. Watson KD, Papageorgiou AC, Jones GT, et al. Low back pain in schoolchildren: occurrence and characteristics. Pain. 2002;97(1–2):87–92.
43. Snodgrass W. Relationship of voiding dysfunction to urinary tract infection and vesicoureteral reflux in children. Urology. 1991;38(4):341–4.
44. Sureshkumar P, Jones M, Cumming R, Craig J. A population based study of 2,856 school-age children with urinary incontinence. J Urol. 2009;181(2):808–15; discussion 815–806
45. Sureshkumar P, Craig JC, Roy LP, Knight JF. Daytime urinary incontinence in primary school children: a population-based survey. J Pediatr. 2000;137(6):814–8.
46. Saedi NA, Schulman SL. Natural history of voiding dysfunction. Pediatr Nephrol. 2003;18(9):894–7.
47. Steinbok P, MacNeily AE, Hengel AR, et al. Filum section for urinary incontinence in children with occult tethered cord syndrome: a randomized, controlled pilot study. J Urol. 2016;195(4 Pt 2):1183–8.
48. McLone DG, La Marca F. The tethered spinal cord: diagnosis, significance, and management. Semin Pediatr Neurol. 1997;4(3):192–208.
49. Warder DE. Tethered cord syndrome and occult spinal dysraphism. Neurosurg Focus. 2001;10(1):e1.
50. Steinbok P, Kariyattil R, MacNeily AE. Comparison of section of filum terminale and non-neurosurgical management for urinary incontinence in patients with normal conus position and possible occult tethered cord syndrome. Neurosurgery. 2007;61(3):550–5; discussion 555–556
51. Steinbok P, Garton HJ, Gupta N. Occult tethered cord syndrome: a survey of practice patterns. J Neurosurg. 2006;104(5 Suppl):309–13.

52. McCullough DC, Levy LM, DiChiro G, Johnson DL. Toward the prediction of neurological injury from tethered spinal cord: investigation of cord motion with magnetic resonance. Pediatr Neurosurg. 1990;16(1):3–7.
53. Levy LM, Di Chiro G, McCullough DC, Dwyer AJ, Johnson DL, Yang SS. Fixed spinal cord: diagnosis with MR imaging. Radiology. 1988;169(3):773–8.
54. Yamada S, Won DJ. Occult tethered cord. J Neurosurg. 2007;106(5 Suppl):411–3; author reply 413–414
55. Biesheuvel C, Barratt A, Howard K, Houssami N, Irwig L. Effects of study methods and biases on estimates of invasive breast cancer overdetection with mammography screening: a systematic review. Lancet Oncol. 2007;8(12):1129–38.
56. Moynihan R, Doust J, Henry D. Preventing overdiagnosis: how to stop harming the healthy. Brit Med J. 2012;e3502:344.
57. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA. 2006;295(18):2164–7.
58. Guthkelch AN. Diastematomyelia with median septum. Brain. 1974;97(4):729–42.
59. Hoffman HJ, Taecholarn C, Hendrick EB, Humphreys RP. Management of lipomyelomeningoceles. Experience at the Hospital for Sick Children, Toronto. J Neurosurg. 1985;62(1):1–8.
60. Lunardi P, Missori P, Gagliardi FM, Fortuna A. Long-term results of the surgical treatment of spinal dermoid and epidermoid tumors. Neurosurgery. 1989;25(6):860–4.
61. Anderson FM. Occult spinal dysraphism: a series of 73 cases. Pediatrics. 1975;55(6):826–35.
62. Kanev PM, Lemire RJ, Loeser JD, Berger MS. Management and long-term follow-up review of children with lipomyelomeningocele, 1952–1987. J Neurosurg. 1990;73(1):48–52.
63. Keating MA, Rink RC, Bauer SB, et al. Neurourological implications of the changing approach in management of occult spinal lesions. J Urol. 1988;140(5 Pt 2):1299–301.
64. Dias MS, Pang D. Split cord malformations. Neurosurg Clin North Am. 1995;6(2):339–58.
65. Tuuha SE, Aziz D, Drake J, Wales P, Kim PC. Is surgery necessary for asymptomatic tethered cord in anorectal malformation patients? J Pediatr Surg. 2004;39(5):773–7.
66. Kulkarni AV, Pierre-Kahn A, Zerah M. Conservative management of asymptomatic spinal lipomas of the conus. Neurosurgery. 2004;54(4):868–73; discussion 873–865
67. Wykes V, Desai D, Thompson DN. Asymptomatic lumbosacral lipomas – a natural history study. Childs Nerv Syst. 2012;28(10):1731–9.
68. Fournier JC, DeRubeis RJ, Hollon SD, et al. Antidepressant drug effects and depression severity: a patient-level meta-analysis. JAMA. 2010;303(1):47–53.
69. Cundy T. Proposed new diagnostic criteria for gestational diabetes – a pause for thought? Diabet Med. 2012;29(2):176–80.
70. Prasad V, Rho J, Cifu A. The diagnosis and treatment of pulmonary embolism: a metaphor for medicine in the evidence-based medicine era. Arch Intern Med. 2012;172(12):955–8.
71. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ. 1996;312(7023):71–2.
72. Every-Palmer S, Howick J. How evidence-based medicine is failing due to biased trials and selective publication. J Eval Clin Pract. 2014;20(6):908–14.
73. Evidence-Based Medicine Working Group. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA. 1992;268(17):2420–5.